

Connecting via Winsock to STN

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***** Welcome to STN International *****

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
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NEWS 4 ZDB will be removed from STN
NEWS 5 US Patent Applications available in IFICDB, IFIPAT, and IFIUDB
NEWS 6 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
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NEWS 9 New e-mail delivery for search results now available
NEWS 10 MEDLINE Reload
NEWS 11 PCTFULL has been reloaded
NEWS 12 FORGE no longer contains STANDARDS file segment
NEWS 13 USAN to be reloaded July 28, 2002;
saved answer sets no longer valid
NEWS 14 Enhanced polymer searching in REGISTRY
NEWS 15 NETFIRST to be removed from STN
NEWS 16 CANCERLIT reload
NEWS 17 PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18 NTIS has been reloaded and enhanced
NEWS 19 Aquatic Toxicity Information Retrieval (AQUIRE)
now available on STN
NEWS 20 IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 21 The MEDLINE file segment of TOXCENTER has been reloaded
NEWS 22 Sequence searching in REGISTRY enhanced
NEWS 23 JAPIO has been reloaded and enhanced
NEWS 24 Experimental properties added to the REGISTRY file
NEWS 25 Indexing added to some pre-1967 records in CA/CAPLUS
NEWS 26 CA Section Thesaurus available in CAPLUS and CA

NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d.
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0a(JP).
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (General Information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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***** STN Columbus *****

FILE 'HOME' ENTERED AT 15:54:33 ON 16 SEP 2002

=> file medline, cancerlit, biosis, confsci, embase, uspatfull
COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL
0.21 0.21
FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 15:54:59 ON 16 SEP 2002

FILE 'CANCERLIT' ENTERED AT 15:54:59 ON 16 SEP 2002

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FILE 'USPATFULL' ENTERED AT 15:54:59 ON 16 SEP 2002
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=> s polyclon? (a) antibody? and librar?

L1 10687 POLYCLON? (A) ANTIBOD? AND LIBRAR?

L2 7077 L1 AND EXPRESSION(A) VECTOR

=> dup rem l2

PROCESSING IS APPROXIMATELY 20% COMPLETE FOR L2

PROCESSING IS APPROXIMATELY 40% COMPLETE FOR L2

PROCESSING IS APPROXIMATELY 59% COMPLETE FOR L2

PROCESSING IS APPROXIMATELY 76% COMPLETE FOR L2

PROCESSING IS APPROXIMATELY 94% COMPLETE FOR L2

PROCESSING COMPLETED FOR L2

L3 6978 DUP REM L2 (99 DUPLICATES REMOVED)

=> d his

(FILE 'HOME' ENTERED AT 15:54:33 ON 16 SEP 2002)

FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT

15:54:59 ON 16 SEP 2002

L1 10687 S POLYCLON? (A) ANTIBOD? AND LIBRAR?

L2 7077 S L1 AND EXPRESSION(A)VECTOR

L3 6978 DUP REM L2 (99 DUPLICATES REMOVED)

=> s variable (a) chain and l3

COMMAND INTERRUPTED

REENTER FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL'

AND TRY AGAIN, OR ENTER '?' FOR MORE INFORMATION.

QUERY PROCESSING INTERRUPTED

The system was temporarily unable to process your query. If this

message appears repeatedly, please notify the Help Desk. Enter 'HELP

STN' for information on contacting the nearest STN Help Desk by

telephone or via SEND in the STNMAIL file.

=> file medline, cancerlit, biosis, confsci, embase, uspatfull

'CANCERLIT' IS NOT A VALID FILE NAME

Enter "HELP FILE NAMES" at an arrow prompt (=>) for a list of files

that are available. If you have requested multiple files, you can

specify a corrected file name or you can enter "IGNORE" to continue

```

accessing the remaining file names entered.
ENTER A FILE NAME OR (IGNORE):cancerlit
COST IN U.S. DOLLARS
FULL ESTIMATED COST
SINCE FILE ENTRY TOTAL
16.93 17.14

FILE 'MEDLINE' ENTERED AT 16:02:49 ON 16 SEP 2002
FILE 'CANCERLIT' ENTERED AT 16:02:49 ON 16 SEP 2002
FILE 'BIOSIS' ENTERED AT 16:02:49 ON 16 SEP 2002
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FILE 'USPATFULL' ENTERED AT 16:02:49 ON 16 SEP 2002
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=> d his
(FILE 'HOME' ENTERED AT 15:54:33 ON 16 SEP 2002)
FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT
15:54:59 ON 16 SEP 2002
L1 10687 S POLYCLON? (A) ANTIBOD? AND LIBRAR?
L2 7077 S L1 AND EXPRESSION(A)VECTOR
L3 6978 DUP REM L2 (99 DUPLICATES REMOVED)
FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT
16:02:49 ON 16 SEP 2002
=> s l3 and variable(a)chain
QUERY PROCESSING INTERRUPTED
The system was temporarily unable to process your query. If this
message appears repeatedly, please notify the Help Desk. Enter "HELP
SIN" for information on contacting the nearest STN Help Desk by
telephone or via SEND in the STNMAIL file.
=>
---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y
COST IN U.S. DOLLARS
FULL ESTIMATED COST
SINCE FILE ENTRY TOTAL
8.15 25.29

STN INTERNATIONAL LOGOFF AT 16:06:10 ON 16 SEP 2002

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Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspal642cxy

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

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NEWS 23 SEP 03 JAPLO has been reloaded and enhanced
NEWS 24 SEP 16 Experimental properties added to the REGISTRY file
NEWS 25 SEP 16 Indexing added to some pre-1967 records in CA/CAPLUS
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FILE 'HOME' ENTERED AT 12:23:05 ON 26 SEP 2002

=> file medline, cancerlit, biosis, confsci, embase, uspatfull
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
0.21 0.21

FULL ESTIMATED COST

FILE 'MEDLINE' ENTERED AT 12:23:48 ON 26 SEP 2002

FILE 'CANCERLIT' ENTERED AT 12:23:48 ON 26 SEP 2002

FILE 'BIOSIS' ENTERED AT 12:23:48 ON 26 SEP 2002

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=> s antibod? and librar?

L1 41608 ANTIBOD? AND LIBRAR?

=> s polyclona?

L2 137092 POLYCLONA?

=> s l2 and l1

L3 15758 L2 AND L1

=> s l3 and phage?

L4 9841 L3 AND PHAGE?

=> s l4 not py=> 1994

'1994' NOT A VALID FIELD CODE

L5 5 FILES SEARCHED...

L5 414 L4 NOT PY=> 1994

=> dup rem

ENTER L# LIST OR (END):15

PROCESSING COMPLETED FOR L5

L6 339 DUP REM L5 (75 DUPLICATES REMOVED)

=> d l6 1-50

L6 ANSWER 1 OF 339 USPATFULL

AN 93:109185 USPATFULL

TI cDNA coding for carcinoembryonic antigen (CEA)

IN Barnett, Thomas R., East Haven, CT, United States

Elting, James J., Madison, CT, United States

Kamarck, Michael E., Bethany, CT, United States

PA Molecular Diagnostics, Inc., West Haven, CT, United States (U.S.

corporation)

PI US 5274087 19931228

AI US 1992-876821 19920429 (7)

RLI Continuation of Ser. No. US 1988-231741, filed on 12 Aug 1988, now

abandoned which is a continuation-in-part of Ser. No. US 1987-60031,

filed on 19 Jun 1987, now abandoned which is a continuation-in-part of

Ser. No. US 1987-16683, filed on 19 Feb 1987, now abandoned which is a

continuation-in-part of Ser. No. US 1986-896361, filed on 13 Aug 1986,
now abandoned

DT Utility
FS Granted
LN.CNT 1207

INCL INCLM: 536/023.500
INCLM: 536/006.000; 435/172.300; 435/320.100; 536/023.500; 536/024.300;
INCLM: 536/024.310; 935/011.000; 935/027.000

NCL INCLM: 536/023.500
INCLM: 536/023.500

IC INCLM: 435/006.000; 435/320.100; 536/024.300; 536/024.310
[5]

ICM: C07H015-12
ICS: C07H021-04; C12N015-00
435/91; 435/172.3; 435/240.1; 435/240.4; 435/252.3; 435/252.33;
435/254.34; 435/6; 435/320.1; 536/27; 536/24.3; 536/24.31; 536/24.5;
935/11; 935/27

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 2 OF 339 USPATFULL
AN 93:108990 USPATFULL
TI Gamma-Interferon-leukotoxin gene fusions and uses thereof
IN Potter, Andrew, Saskatoon, Canada
Campos, Manuel, Saskatoon, Canada
Hughes, Huw P. A., Saskatoon, Canada
PA University of Saskatchewan, Saskatoon, Canada (non-U.S. corporation)
Ciba-Geigy Canada, Ltd., Saskatoon, Canada (non-U.S. corporation)
PI US 5273889 19911016 (7)
AI US 1991-777715 19911016 (7)
RLI Continuation-in-part of Ser. No. US 1990-571301, filed on 22 Aug 1990
DT Utility
FS Granted
LN.CNT 1727

INCL INCLM: 435/069.510
INCLM: 435/069.500; 435/069.520; 435/069.700; 435/172.300; 435/243.000;
INCLM: 435/252.300; 435/320.100; 435/811.000; 536/023.100

NCL INCLM: 435/069.510
INCLM: 435/069.500; 435/069.520; 435/069.700; 435/243.000; 435/252.300;
INCLM: 435/320.100; 435/811.000; 536/023.100

IC [5]

ICM: C12N015-23
ICS: C12N015-19; C07H015-12
435/69.5; 435/69.51; 435/69.52; 435/69.7; 435/252.3; 435/243; 435/172.3;
435/320.1; 435/81; 536/27; 536/23.1

EXF 435/320.1; 435/81; 536/27; 536/23.1

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 3 OF 339 USPATFULL
AN 93:108986 USPATFULL
TI Polypeptides, antigens or vaccines protective against babesiosis
IN Gale, Kevin G., Brisbane, Australia
Waltisbuhl, David J., Queensland, Australia
Wright, Ian G., Brisbane, Australia
Goodger, Brian V., New South Wales, Australia
PA Commonwealth Scientific & Industrial, United States (non-U.S. corporation)
PI US 5273884 19911228
AI US 1990-470284 19900125 (7)
PRAI AU 1989-4427 19890125
AU 1989-7722 19891116
DT Utility
FS Granted
LN.CNT 1771

INCL INCLM: 435/007.100
INCLM: 424/088.000; 435/007.220; 435/069.100; 530/388.100; 530/388.600;
INCLM: 530/350.000; 536/023.100

NCL INCLM: 424/191.100
INCLM: 424/256.100; 424/270.100; 435/007.220; 435/069.100; 530/350.000;
INCLM: 530/388.100; 530/388.600; 536/023.100

IC [5]

ICM: G01N033-53
ICS: C07K015-28; A61K039-00; C07H021-02
435/6; 435/71.1; 435/77.2; 435/69.1; 435/71.1; 435/71.2; 435/71.2.1; 435/172.1;
435/172.2; 435/172.3; 435/240.26; 435/240.27; 435/252.3; 435/252.33;
435/77.22; 436/501; 436/548; 436/519; 436/63; 530/387; 530/809; 536/26;
536/27; 536/28; 536/29; 536/23.1; 935/65; 935/95; 935/102; 935/106;
424/88

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 4 OF 339 USPATFULL
AN 93:108848 USPATFULL
TI Bacillus thuringiensis isolates active against phthiraptera pests
IN Payne, Jewel M., San Diego, CA, United States
Hickie, Leslie A., San Diego, CA, United States
PA Mycogen Corporation, San Diego, CA, United States (U.S. corporation)
PI US 5273746 19931228
AI US 1992-828788 19920129 (7)
DT Utility
FS Granted
LN.CNT 1775

INCL INCLM: 424/093.000L
INCLM: 435/252.500; 435/252.310; 536/023.710; 514/002.000

NCL INCLM: 424/093.461
INCLM: 424/093.200; 435/252.310; 435/252.500; 514/002.000; 536/023.710

IC [5]

ICM: A01N063-04
ICS: A01N037-18; C07H021-04
424/93L; 424/DIG.10; 435/252.31; 435/252.5; 514/2; 536/27

EXF 424/93L; 424/DIG.10; 435/252.31; 435/252.5; 514/2; 536/27

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 5 OF 339 USPATFULL
AN 93:107133 USPATFULL
TI DNA sequences encoding vascular cell adhesion molecules (VCAMS)
IN Hession, Catherine A., South Weymouth, MA, United States
Lobb, Roy R., Westwood, MA, United States
Goelz, Susan E., Winchester, MA, United States
Osborn, Laurelee, Brighton, MA, United States
Benjamin, Christopher D., Beverly, MA, United States
Rosa, Margaret D., Winchester, MA, United States
PA Biogen, Inc., Cambridge, MA, United States (U.S. corporation)
PI US 5272263 19931221
AI US 1989-452675 19891218 (7)
RLI Continuation-in-part of Ser. No. US 1989-359516, filed on 1 Jun 1989,
now abandoned which is a continuation-in-part of Ser. No. US
1989-345151, filed on 28 Apr 1989

DT Utility
FS Granted
LN.CNT 2440

INCL INCLM: 536/023.500
INCLM: 530/380.000; 435/069.600; 435/320.100

NCL INCLM: 536/023.500
INCLM: 435/069.600; 435/320.100; 530/380.000

IC [5]

ICM: C07K013-00
ICS: C12N015-00; C12P021-06
435/69.1; 435/69.9; 435/320.1; 530/380; 536/27

EXF 435/69.1; 435/69.9; 435/320.1; 530/380; 536/27

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 6 OF 339 USPATFULL
AN 93:106950 USPATFULL

TI CDNA encoding the type I iodothyronine 5'-deiodinase
IN Larsen, P. Reed, Brookline, MA, United States
PA Berry, Marla J., Brighton, MA, United States
Brigham and Women's Hospital, Boston, MA, United States (U.S.)
PI US 5272078 19931221
AI US 1992-828790 19920129 (7)
RLI Continuation-in-part of Ser. No. US 1991-757024, filed on 3 Sep 1991,
now abandoned which is a continuation-in-part of Ser. No. US
1991-647657, filed on 29 Jan 1991, now abandoned
DT Utility
FS Granted
LN.CNT 2500
INCL INCLM: 435/189.000
INCLS: 435/069.100; 435/172.100; 435/252.300; 435/320.100; 536/023.200;
536/024.100; 935/009.000; 935/011.000; 935/022.000; 935/044.000;
935/066.000; 935/079.000
NCL NCLM: 435/189.000
NCLS: 435/069.100; 435/252.300; 435/320.100; 536/023.200; 536/024.100
IC [5]
ICM: G12N015-53
ICS: G12N015-11; G12N015-63; C12P021-00
EXF 435/69.1; 435/252.3; 435/320.1; 435/187; 536/27; 536/23.2; 536/24.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L6 ANSWER 7 OF 339 USPATFULL
AN 93:105101 USPATFULL
TI Nucleic acids encoding fragments of hematopoietic stem cell receptor
fik-2
IN Lemischka, Ihor R., Princeton, NJ, United States
PA The Trustees of Princeton University, Princeton, NJ, United States (U.S.)
PI US 5270458 19931214
AI US 1992-977451 19921119 (7)
RLI Continuation-in-part of Ser. No. US 1992-975049, filed on 12 Nov 1992
which is a continuation-in-part of Ser. No. US 1992-906397, filed on 26
Jun 1992 which is a continuation-in-part of Ser. No. US 1991-813593,
filed on 24 Dec 1991, now patented, Pat. No. US 5185438 which is a
continuation-in-part of Ser. No. US 1991-793065, filed on 15 Nov 1991,
now abandoned which is a continuation-in-part of Ser. No. US
1991-728913, filed on 28 Jun 1991, now abandoned which is a
continuation-in-part of Ser. No. US 1991-679666, filed on 2 Apr 1991,
now abandoned
DT Utility
FS Granted
LN.CNT 1919
INCL INCLM: 536/023.500
INCLS: 435/069.100; 435/320.100; 530/350.000; 530/403.000
NCL NCLM: 536/023.500
NCLS: 435/069.100; 435/320.100; 530/350.000; 530/403.000
IC [5]
ICM: C07H021-00
EXF 536/23.5; 530/350; 530/387.1; 530/846; 435/240.2; 435/69.1; 435/172.1;
435/320.1; 514/2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L6 ANSWER 8 OF 339 USPATFULL
AN 93:105095 USPATFULL
TI Pure gila maturation factor
IN Lim, Ramon, Iowa City, IA, United States
Kaplan, Ruth, West Chester, PA, United States
Jaye, Michael, Glenside, PA, United States
Rhône-Poulenc Rorer Pharmaceuticals Inc., Collegeville, PA, United
States (U.S. corporation)
PA

PI US 5270452 19931214
AI US 1991-785185 19911031 (7)
RLI Continuation of Ser. No. US 1991-692772, filed on 26 Apr 1991, now
abandoned which is a continuation of Ser. No. US 1988-276847, filed on
28 Nov 1988, now abandoned
DT Utility
FS Granted
LN.CNT 506
INCL INCLM: 530/399.000
INCLS: 530/350.000; 435/172.300; 435/252.300; 435/320.100; 435/069.100
NCL NCLM: 530/399.000
NCLS: 435/069.100; 435/252.300; 435/320.100; 435/466.000; 435/483.000;
435/485.000; 435/488.000; 530/350.000
IC [5]
ICM: C07K013-00
ICS: C12P021-02; C12N015-00
EXF 435/172.3; 435/69.1; 530/399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L6 ANSWER 9 OF 339 USPATFULL
AN 93:104845 USPATFULL
TI Human mannose-binding protein
IN Ezekowitz, Raymond A. B., Boston, MA, United States
PA The Children's Medical Center Corporation, Boston, MA, United States
(U.S. corporation)
PI US 5270199 19931214
AI US 1992-831619 19920206 (7)
RLI Continuation of Ser. No. US 1989-417822, filed on 5 Oct 1989 which is a
continuation-in-part of Ser. No. US 1987-87628, filed on 20 Aug 1987,
now abandoned
DT Utility
FS Granted
LN.CNT 668
INCL INCLM: 435/240.200
INCLS: 435/069.100; 435/172.300; 435/320.100; 435/235.100; 435/252.300;
435/252.330; 435/254.110; 435/254.200; 536/023.400; 536/023.500;
530/350.000; 935/018.000; 935/027.000; 935/032.000; 935/034.000;
935/038.000; 935/055.000; 935/062.000; 935/070.000; 935/072.000
NCL NCLM: 435/372.100
NCLS: 435/069.100; 435/235.100; 435/252.300; 435/252.330; 435/254.110;
435/254.200; 435/320.100; 530/350.000; 536/023.400; 536/023.500
IC [5]
ICM: C12N005-00
ICS: C12N015-00; C12N007-00; C12N001-21; C12N001-16; C12N001-18;
C12P021-02; C12P019-34; C02K003-00; C07H015-12
EXF 435/69.1; 435/91; 435/172.3; 435/235.1; 435/320.1; 435/240.2; 435/252.3;
435/252.33; 435/255; 435/256; 536/27; 530/350; 535/18; 535/27; 535/32;
535/34; 535/38; 535/55; 535/62; 535/70; 535/72
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
L6 ANSWER 10 OF 339 USPATFULL
AN 93:102938 USPATFULL
TI Overexpression of phytochrome in transgenic plants
IN Hershey, Howard P., West Chester, PA, United States
Keller, Janis M., Wilmington, DE, United States
PA E. I. Du Pont de Nemours and Company, Wilmington, DE, United States
(U.S. corporation)
PI US 5268526 19931207
AI US 1988-284422 19881214 (7)
RLI Continuation-in-part of Ser. No. US 1988-226344, filed on 29 Jul 1988,
now abandoned
DT Utility
FS Granted
LN.CNT 1928

INCL INCLM: 800/205.000
INCL: 800/255.000; 800/DIG.009; 435/320.100; 935/035.000; 935/067.000
NCL NCLM: 800/298.000
NCL: 435/320.100; 800/305.000; 800/306.000; 800/307.000; 800/310.000;
800/311.000; 800/312.000; 800/313.000; 800/314.000; 800/317.000;
800/317.100; 800/317.200; 800/317.300; 800/317.400; 800/318.000;
800/323.000; 800/323.100; 800/323.200; 800/323.300
IC [5]
ICM: A01H004-00
ICS: C12N015-29
EXF 800/1; 800/200; 800/205; 800/250; 800/255; 800/DIG.9; 435/66; 435/172.1;
435/172.3; 435/320.1; 435/69.1; 935/9; 935/10; 935/30; 935/35; 935/47;
935/64; 935/67; 047/58
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 11 OF 339 USPATFULL
AN 93:102708 USPATFULL
TI Mammalian adipocyte protein p154, nucleic acids coding therefor and uses
thereof
IN Sertero, Ginette, Lake Placid, NY, United States
PA W. Alton Jones Cell Science Center, Inc., Lake Placid, NY, United States
(U.S. corporation)
PI US 5268295 19931207
AI US 1991-708038 19910531 (7)
DT Utility
FS Granted
LN.CNT 2018
INCL INCLM: 435/252.300
INCL: 435/069.100; 435/070.100; 435/070.300; 435/071.100; 435/172.300;
435/240.200; 435/320.100; 536/023.500; 935/011.000; 935/027.000;
935/056.000; 935/066.000
NCL NCLM: 435/252.300
NCL: 435/069.100; 435/070.100; 435/070.300; 435/071.100; 435/320.100;
536/023.500
IC [5]
ICM: C12N015-12
ICS: C12N015-63
EXF 536/27; 536/23.5; 435/69.1; 435/70.1; 435/70.3; 435/71.1; 435/172.3;
435/240.2; 435/252.3; 435/320.1; 935/8; 935/11; 935/12; 935/24; 935/27;
935/56; 935/66
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 12 OF 339 USPATFULL
AN 93:102688 USPATFULL
TI Vitamin K-dependent carboxylase
IN Stafford, Darrel W., Carrboro, NC, United States
Wu, Sheue-Mei, Carrboro, NC, United States
PA The University of North Carolina at Chapel Hill, Chapel Hill, NC, United
States (U.S. corporation)
PI US 5268275 19931207
AI US 1991-756250 19910909 (7)
RLI Continuation-in-part of Ser. No. US 1991-697427, filed on 8 May 1991,
now abandoned
DT Utility
FS Granted
LN.CNT 1386
INCL INCLM: 435/691.000
INCL: 435/069.600; 435/172.100; 435/172.300; 435/240.200; 435/252.300;
435/320.100; 536/023.200; 935/010.000; 935/034.000; 935/049.000
NCL NCLM: 435/069.100
NCL: 435/069.600; 435/232.000; 435/252.300; 435/320.100; 435/352.000;
435/354.000; 435/358.000; 435/366.000; 536/023.200
IC [5]
ICM: C12P021-00

ICS: C12N009-88; C12N001-00; C12N005-00; C12N015-60; C12N015-67;
C07H021-04
EXF 435/69.1; 435/69.6; 435/110; 435/232; 435/172.1; 435/240.2; 435/320.1;
435/252.3; 435/240.1; 536/27; 536/23.2; 935/10; 935/34; 935/49
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 13 OF 339 USPATFULL
AN 93:100861 USPATFULL
TI Polynucleotide sequence for production of glucose oxidase in recombinant
systems
IN Rosenberg, Steven, Oakland, CA, United States
PA Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
PI US 5266688 19931130
AI US 1992-848406 19920306 (7)
RLI Continuation of Ser. No. US 1989-366377, filed on 19 Jun 1989, now
patented, Pat. No. US 5094951 which is a continuation of Ser. No. US
1988-209530, filed on 21 Jun 1988, now abandoned
DT Utility
FS Granted
LN.CNT 2005
INCL INCLM: 536/023.200
INCL: 435/320.100
NCL NCLM: 536/023.200
NCL: 435/320.100
IC [5]
ICM: C12N015-53
EXF 536/27; 536/23.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 14 OF 339 USPATFULL
AN 93:100856 USPATFULL
TI Osteogenic proteins
IN Oopermann, Hermann, Medway, MA, United States
Oskaynak, Engin, Milford, MA, United States
Kuberasamath, Thangavel, Medway, MA, United States
Rueger, David C., Hopkinton, MA, United States
Pang, Roy H. L., Medway, MA, United States
PA Stryker Corporation, Kalamazoo, MI, United States (U.S. corporation)
PI US 5266683 19931130
AI US 1992-841646 19920221 (7)
RLI Continuation-in-part of Ser. No. US 1992-827052, filed on 28 Jan 1992,
now patented, Pat. No. US 5250302 Ser. No. US 1990-579865,
filed on 7 Oct 1990, now patented, Pat. No. US 5108753 Ser. No. Ser. No.
US 1990-621849, filed on 4 Dec 1990, now abandoned Ser. No. Ser. No. US
1990-621988, filed on 4 Dec 1990, now abandoned Ser. No. Ser. No. US
1991-810540, filed on 20 Dec 1991, now abandoned Ser. No. Ser. No. US
1990-569920, filed on 20 Aug 1990, now abandoned Ser. No. Ser. No. US
1990-600024, filed on 18 Oct 1990, now abandoned Ser. No. Ser. No. US
1990-599543, filed on 18 Oct 1990, now patented, Pat. No. US 5162114 And
Ser. No. US 1990-483913, filed on 22 Feb 1990, now patented, Pat. No. US
5171574, said Ser. No. 827052 which is a division of Ser. No. US
1988-179406, filed on 8 Apr 1988, now patented, Pat. No. US 4968590,
said Ser. No. 579865 which is a division of Ser. No. 179406, said
Ser. No. 621849 which is a division of Ser. No. US 1988-232630, filed
on 15 Aug 1988, now abandoned which is a continuation-in-part of Ser.
No. 179406, said Ser. No. 621988 which is a continuation of Ser. No.
US 1989-315342, filed on 23 Feb 1989, now patented, Pat. No. US 5011691
which is a continuation-in-part of Ser. No. 232630, said Ser. No.
810560 which is a continuation of Ser. No. US 1991-660162, filed on 22
Feb 1991, now abandoned which is a continuation of Ser. No. US
1989-422699, filed on 17 Oct 1989, now abandoned which is a
continuation-in-part of Ser. No. 315342, said Ser. No. 569920
which is a continuation-in-part of Ser. No. 422699 And Ser. No.

483913 which is a continuation-in-part of Ser. No. US 1989-422613, filed on 17 Oct 1989, now patented, Pat. No. US 4975526 which is a continuation-in-part of Ser. No. 315342, said Ser. No. 600024 which is a continuation-in-part of Ser. No. 569920, said Ser. No. 599543 which is a continuation-in-part of Ser. No. 569920 which is a continuation-in-part of Ser. No. 569920

DT Utility
FS Granted
LN.CNT 4144
INCL INCLM: 530/326.000
INCLS: 530/327.000; 530/328.000; 530/350.000; 530/395.000; 530/840.000
NCL NCLM: 530/326.000
NCLS: 530/327.000; 530/328.000; 530/350.000; 530/395.000; 530/840.000
IC [5]
ICM: A61K037-02
ICS: C07K005-00; C07K007-00; C07K015-00
EXF 530/326; 530/327; 530/328; 530/395; 530/840; 530/300; 530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 15 OF 339 USPATFULL
AN 93:100641 USPATFULL
TI .alpha.-i-antichymotrypsin, analogues and methods of production
IN Rubin, Harvey, Philadelphia, PA, United States
Wang, Zhi M., Philadelphia, PA, United States
Cooperman, Barry S., Penn Valley, PA, United States
Schecter, Norman, Philadelphia, PA, United States
The Trustees of the University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)
PA US 5266465 19931130
PI US 1991-735322 19910724 (7)
AI US 1991-735322 19910724 (7)
RLI Division of Ser. No. US 1989-370704, filed on 23 Jun 1989, now patented, Pat. No. US 5079336
DT Utility
FS Granted
LN.CNT 853
INCL INCLM: 435/069.200
INCLS: 435/069.100; 435/172.100; 435/172.300; 435/213.000; 530/350.000
NCL NCLM: 435/069.200
NCLS: 435/069.100; 435/213.000; 530/350.000
IC [5]
ICM: C07K003-00
ICS: C12P021-02; C12N015-09; A61K045-05
EXF 435/69.1; 435/69.2; 435/172.1; 435/172.3; 435/320.1; 435/213; 530/380; 530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 16 OF 339 USPATFULL
AN 93:100493 USPATFULL
TI Insect-specific paralytic neurotoxin genes for use in biological insect control: methods and compositions
IN Tomalski, Michael D., Athens, GA, United States
Miller, Lois K., Athens, GA, United States
PA University of Georgia Research Foundation, Inc., Athens, GA, United States (U.S. corporation)
PI US 5266317 19931130
AI US 1990-593657 19901004 (7)
DT Utility
FS Granted
LN.CNT 2085
INCL INCLM: 424/093.000T
INCLS: 536/023.500; 435/235.100; 435/069.100; 435/172.300; 435/320.100
NCL NCLM: 424/093.200
NCLS: 424/093.600; 435/069.100; 435/235.100; 435/320.100; 536/023.500
IC [5]

ICM: C12N007-01
ICS: C12N015-12
EXF 536/27; 536/93.5; 935/36; 435/69.1; 435/235.1; 435/320.1; 435/172.3; 424/93; 434/93T
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 17 OF 339 USPATFULL
AN 93:98501 USPATFULL
TI Polypeptide of a human crypto-related gene, CR-3
IN Solomon, David S., Germantown, MD, United States
Persico, Maria G., Naples, Italy
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5264557 19931123
AI US 1991-749001 19910823 (7)
DT Utility
FS Granted
LN.CNT 686
INCL INCLM: 530/399.000
INCLS: 530/350.000; 530/387.700; 530/387.900; 435/006.000; 435/069.100; 435/007.230; 536/023.510
NCL NCLM: 530/399.000
NCLS: 435/006.000; 435/007.230; 435/069.100; 530/350.000; 530/387.700; 530/387.900; 536/023.510
IC [5]
ICM: C07K003-00
ICS: A61K037-24; C12P021-06; C07H015-12
EXF 435/69.1; 435/67; 435/7.23; 530/350; 530/387; 530/399; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 18 OF 339 USPATFULL
AN 93:98498 USPATFULL
TI Platelet cell adhesion molecule and variants thereof
IN Newman, Peter J., Shorewood, WI, United States
PA The Blood Center of Southeastern Wisconsin, Inc., Milwaukee, WI, United States (U.S. corporation)
PI US 5264554 19931123
AI US 1990-466140 19900119 (7)
DT Utility
FS Granted
LN.CNT 772
INCL INCLM: 530/387.100
INCLS: 530/395.000; 530/350.000; 530/324.000; 435/069.100; 424/085.800
NCL NCLM: 530/387.100
NCLS: 435/069.100; 530/324.000; 530/350.000; 530/387.900; 530/395.000; 536/023.500
IC [5]
ICM: C07K013-00
ICS: C07K009-00; C07K015-14; A61K039-00
EXF 530/387; 530/388; 530/395; 530/330; 530/329; 530/328; 530/327; 530/326; 530/325; 530/324; 530/350; 530/387.1; 514/8; 435/69.1; 424/85.8
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 19 OF 339 USPATFULL
AN 93:98494 USPATFULL
TI Human anti-inflammatory phospholipase inhibitor protein
IN Johnson, Lorin K., Pleasanton, CA, United States
PA Longenecker, John P., Mt. View, CA, United States
PI Scios Nova Inc., Mountain View, CA, United States (U.S. corporation)
US 5264550 19931123
US 1992-871577 19920420 (7)
AI Continuation of Ser. No. US 1990-538692, filed on 14 Jun 1990, now abandoned which is a continuation of Ser. No. US 1986-883598, filed on 9

Jul 1986, now abandoned which is a continuation-in-part of Ser. No. US 1985-723046, filed on 15 Apr 1985, now abandoned

DT Utility
FS Granted
LN.CNT 1582
INCL INCLM: 530/350.000
INCLS: 530/395.000; 530/851.000; 435/692.000
NCL INCLM: 530/350.000
NCLS: 435/069.200; 530/395.000; 530/851.000
IC [5]
ICM: C07K013-00
EXF 530/350; 530/395; 530/851; 435/69.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 20 OF 339 USPATFULL
AN 93:96243 USPATFULL
TI cDNA probe differentiating normal and cancer tissues
IN Sager, Ruth, Brookline, MA, United States
Lee, Sam W., Boston, MA, United States
Tomasetto, Catherine, Boston, MA, United States
Dana-Farber Cancer Institute, Inc., Boston, MA, United States (U.S. corporation)

PI US 5262528 19931116
AI US 1991-662198 19910228 (7)
DT Utility
FS Granted
LN.CNT 306
INCL INCLM: 536/024.310
INCLS: 435/172.300; 435/252.300
NCL INCLM: 536/024.310
NCLS: 435/252.300
IC [5]
ICM: C12N015-11
EXF 536/27; 536/24.31; 530/300; 530/828; 530/387.7; 435/172.3; 435/240.2;
435/252.3
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 21 OF 339 USPATFULL
AN 93:96237 USPATFULL
TI Receptor for oncostatin M and leukemia inhibitory factor
IN Gearing, David P., Seattle, WA, United States
PA Immunex Corporation, Seattle, WA, United States (U.S. corporation)

PI US 5262522 19931116
AI US 1991-797556 19911122 (7)
DT Utility
FS Granted
LN.CNT 2133
INCL INCLM: 530/350.000
INCLS: 435/069.700; 435/252.300; 435/370.100
NCL INCLM: 530/350.000
NCLS: 435/069.700; 435/252.300; 435/320.100
IC [5]
ICM: C07K013-00
ICS: C12N015-62
EXF 435/69.1; 435/69.7; 530/350; 530/387; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 22 OF 339 USPATFULL
AN 93:96042 USPATFULL
TI Host transformed with yeast gene and ubiquitin/polypeptide fusions
IN Liu, Chung-Cheng, Foster City, CA, United States
Miller, Harvey I., Pleasant Hill, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S.

corporation)
PI US 5262322 19931116
AI US 1991-694522 19910430 (7)
RLI Division of Ser. No. US 1988-284281, filed on 14 Dec 1988, now patented,
Pat. No. US 5108919 which is a continuation-in-part of Ser. No. US
1988-210909, filed on 24 Jun 1988, now patented, Pat. No. US 5156968

DT Utility
FS Granted
LN.CNT 2176
INCL INCLM: 435/252.330
INCLS: 435/069.700; 435/172.300; 435/195.000; 435/224.000; 435/252.300;
435/320.100; 536/023.200; 536/023.400
NCL INCLM: 435/252.330
NCLS: 435/069.700; 435/195.000; 435/224.000; 435/252.300; 435/320.100;
536/023.200; 536/023.400
IC [5]
ICM: C12N001-21
EXF 435/252.33; 435/252.3; 435/69.7; 435/172.3; 435/195; 435/224; 435/320.1;
536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 23 OF 339 USPATFULL
AN 93:96039 USPATFULL
TI Method for obtaining bone marrow free of tumor cells using transforming
growth factor beta-3
IN Wata, Kenneth K., Westbury, NY, United States
Foulkes, J. Gordon, Huntington, NY, United States
Dijke, Peter T., Port Washington, NY, United States
Haley, John D., Great Neck, NY, United States
Oncogene Science, Inc., Uniondale, NY, United States (U.S. corporation)

PI US 5262319 19931116
AI US 1990-543341 19900625 (7)
RLI Continuation-in-part of Ser. No. US 1989-353410, filed on 17 May 1989,
now abandoned which is a continuation-in-part of Ser. No. US
1988-183824, filed on 20 Apr 1988, now abandoned which is a
continuation-in-part of Ser. No. US 1987-111022, filed on 20 Oct 1987,
which is a continuation-in-part of Ser. No. US 1986-922121, filed on 20
Oct 1986, now abandoned which is a continuation-in-part of Ser. No. US
1986-847931, filed on 7 Apr 1986, now abandoned which is a
continuation-in-part of Ser. No. US 1985-725003, filed on 19 Apr 1985,
now abandoned

DT Utility
FS Granted
LN.CNT 1446
INCL INCLM: 435/240.200
INCLS: 435/240.250; 530/399.000
NCL INCLM: 435/378.000
NCLS: 530/399.000
IC [5]
ICM: C12N005-08
ICS: C07K015-14
EXF 435/240.2; 435/240.21; 435/240.25; 514/2; 514/8; 514/25; 530/395;
530/399
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 24 OF 339 USPATFULL
AN 93:95898 USPATFULL
TI Recombinant viruses encoding the human melanoma-associated antigen
IN Brown, Joseph P., Seattle, WA, United States
Escin, Charles D., Bainbridge Island, WA, United States
Plozman, Gregory D., Seattle, WA, United States
Rose, Timothy M., Seattle, WA, United States
Hellstrom, Karl E., Seattle, WA, United States
Hellstrom, Ingegerd, Seattle, WA, United States

Purchio, Anthony F., Seattle, WA, United States
Hu, Shiu-Lok, Redmond, WA, United States
Pennathur, Sridhar, Seattle, WA, United States
Oncogen, Seattle, WA, United States (U.S. corporation)
US 5262177 19931116
US 1987-7230 19870127 (7)
Continuation-in-part of Ser. No. US 1986-827113, filed on 7 Feb 1986,
now abandoned
DT Utility
FS Granted
LN.CNT 1993
LNCL INCLM: 424/089.000
INCL INCLM: 435/069.300; 435/172.300; 435/235.100; 435/320.100; 435/252.300;
INCL INCLM: 435/252.330; 435/240.200; 536/023.500; 530/350.000; 835/009.000;
INCL INCLM: 835/032.000; 835/041.000; 835/057.000; 835/065.000; 835/070.000;
INCL INCLM: 835/073.000
NCL INCLM: 435/235.100
NCL INCLM: 424/185.100; 424/199.100; 424/232.100; 435/069.300; 435/252.300;
INCL INCLM: 435/252.330; 435/320.100; 435/362.000; 530/350.000; 536/023.500
IC [5]
ICM: A61K039-12
ICS: C12P021-02; C12P019-34; C12N015-00; C12N007-00; C12N005-00;
C12N001-21; C12N001-16
EXF 435/68; 435/70; 435/172.1; 435/172.3; 435/235; 435/236; 435/320;
435/69.3; 435/91; 435/235.1; 435/320.1; 435/252.33; 435/255; 435/256;
435/240.2; 424/89; 536/27; 530/350; 835/9; 835/32; 835/41; 835/57;
835/65; 835/70; 835/73
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 25 OF 339 USPATFULL
AN 93:93905 USPATFULL
TI Antigenic epitopes present on membrane-bound but not secreted IgE
IN Chang, Tse-wen, Houston, TX, United States
PA Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI US 5260416 19931109
AI US 1990-468766 19900123 (7)
RLI Continuation-in-part of Ser. No. US 1989-369625, filed on 21 Jun 1989,
now abandoned which is a continuation-in-part of Ser. No. US
1988-272243, filed on 16 Nov 1988, now patented, Pat. No. US 5091313
which is a continuation-in-part of Ser. No. US 1988-229178, filed on 5
Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US
1988-226421, filed on 29 Jul 1988 which is a continuation-in-part of
Ser. No. US 1987-140036, filed on 31 Dec 1987, now abandoned
DT Utility
FS Granted
LN.CNT 859
LNCL INCLM: 530/327.000
INCL INCLM: 530/387.200; 530/387.300; 530/388.730; 530/862.000; 530/868.000;
INCL INCLM: 424/085.800
NCL INCLM: 530/327.000
NCL INCLM: 424/131.100; 424/139.100; 424/140.100; 424/153.100; 424/805.000;
INCL INCLM: 424/810.000; 530/387.200; 530/387.300; 530/388.730; 530/862.000;
INCL INCLM: 530/868.000
IC [5]
ICM: C07K007-08
ICS: C07K017-02
EXF 530/327; 530/388
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 26 OF 339 USPATFULL
AN 93:93760 USPATFULL
TI Odorant-binding protein from rat
IN Snyder, Solomon H., Baltimore, MD, United States
Pevsner, Jonathan, Baltimore, MD, United States

PA Reed, Randall, Baltimore, MD, United States
The Johns Hopkins University, Baltimore, MD, United States (U.S.
corporation)
PI US 5260270 19931109
AI US 1991-730074 19910715 (7)
RLI Division of Ser. No. US 1990-628429, filed on 17 Dec 1990 which is a
division of Ser. No. US 1990-492792, filed on 13 Mar 1990 which is a
division of Ser. No. US 1988-175180, filed on 30 Mar 1988, now patented,
Pat. No. US 5030722, issued on 9 Jul 1991
DT Utility
FS Granted
LN.CNT 839
LNCL INCLM: 514/002.000
INCL INCLM: 514/012.000; 530/350.000; 935/107.000
NCL INCLM: 514/002.000
NCL INCLM: 514/012.000; 530/350.000
IC [5]
ICM: A61K037-02
ICS: C07K013-00
EXF 436/503; 436/501; 512/2; 512/4; 514/2; 514/12; 530/350; 935/107
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 27 OF 339 USPATFULL
AN 93:93713 USPATFULL
TI Methods for detection of human gamma gamma. T cell receptor
IN Brenner, Michael B., Ashland, MA, United States
Strominger, Jack L., Lexington, MA, United States
Seidman, John G., Milton, MA, United States
IP, Stephen H., Framingham, MA, United States
Kangel, Michael S., Newtonville, MA, United States
President & Fellows of Harvard College, Boston, MA, United States (U.S.
corporation)
Dana Farber Cancer Institute & T Cell Diagnostics, Inc., Boston, MA,
United States (U.S. corporation)
PI US 5260223 19931109
AI US 1988-187698 19880429 (7)
RLI Continuation-in-part of Ser. No. US 1987-115256, filed on 29 Oct 1987,
now patented, Pat. No. US 5024940, issued on 18 Jun 1991 which is a
continuation-in-part of Ser. No. US 1987-16252, filed on 19 Feb 1987
which is a continuation-in-part of Ser. No. US 1986-882100, filed on 3
Jul 1986, now abandoned
DT Utility
FS Granted
LN.CNT 1745
LNCL INCLM: 436/501.000
INCL INCLM: 435/007.100; 435/007.240; 435/172.200; 435/240.270; 436/506.000;
INCL INCLM: 436/518.000; 436/548.000; 436/064.000; 530/387.900; 530/388.220;
INCL INCLM: 530/388.750; 530/350.000; 536/023.500
NCL INCLM: 436/501.000
NCL INCLM: 435/007.100; 435/007.240; 436/064.000; 436/506.000; 436/518.000;
INCL INCLM: 436/548.000; 530/350.000; 530/387.900; 530/388.220; 530/388.750;
INCL INCLM: 536/023.500
IC [5]
ICM: G01N033-566
EXF 435/7; 435/172.2; 435/240.27; 435/69.6; 435/7.1; 435/7.23; 436/501;
436/506; 436/518; 436/548; 436/811; 436/813; 436/84; 530/350; 530/387;
530/395; 530/828; 530/829; 935/110
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 28 OF 339 USPATFULL
AN 93:93700 USPATFULL
TI Nucleic acids encoding dystrophin-associated proteins
IN Campbell, Kevin P., Iowa City, IA, United States
Ibraghimov-Beskrovnya, Oxana, Iowa City, IA, United States

Ervasti, James M., Iowa City, IA, United States
 Leveille, Cynthia J., Iowa City, IA, United States
 University of Iowa Research Foundation, Oakdale, IA, United States (U.S. corporation)
 PA US 5260209 19931109
 PI US 1992-841654 19920220 (7)
 RLI Continuation-in-part of Ser. No. US 1990-527583, filed on 23 May 1990, now patented, Pat. No. US 5187063
 DT Utility
 FS Granted
 LN.CNT 1820
 INCL INCLM: 435/240.200
 INCLS: 435/069.100; 435/070.300; 435/071.100; 435/071.200; 435/172.300; 435/252.300; 435/252.300; 435/320.100; 536/023.500; 536/023.500; 935/011.000; 935/027.000; 935/056.000; 530/350.000
 NCL NCLM: 435/325.000
 NCLS: 435/069.100; 435/070.300; 435/071.100; 435/071.200; 435/252.300; 435/320.100; 530/350.000; 536/023.500
 IC [5]
 ICM: C12N015-12
 ICS: C12N015-74; C12N015-79
 EXF 435/69.1; 435/70.3; 435/71.1; 435/71.2; 435/172.3; 435/240.2; 435/252.3; 435/320.1; 536/27; 536/23.5; 530/380; 935/11; 935/27; 935/56
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L6 ANSWER 29 OF 339 USPATFULL
 AN 93:93691 USPATFULL
 TI Isolated DNA encoding an insulin receptor substrate
 IN Kahn, C. Ronald, West Newton, MA, United States
 White, Morris F., West Roxbury, MA, United States
 Rothenberg, Paul L., Naberth, PA, United States
 Joslin Diabetes Center, Inc., Boston, MA, United States (U.S. corporation)
 PA US 5260200 19931109
 PI US 1992-962023 19921015 (7)
 RLI Continuation of Ser. No. US 1991-643982, filed on 18 Jan 1991, now abandoned
 DT Utility
 FS Granted
 LN.CNT 2797
 INCL INCLM: 435/068.100
 INCLS: 435/252.300; 435/320.100; 530/350.000; 536/023.500
 NCL NCLM: 435/069.100
 NCLS: 435/252.300; 435/320.100; 530/350.000; 536/023.500
 IC [5]
 ICM: C07K013-00
 ICS: C12N015-12; C12N015-63
 EXF 435/69.1; 435/252.3; 435/330.1; 530/350; 536/27
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L6 ANSWER 30 OF 339 USPATFULL
 AN 93:91549 USPATFULL
 TI Fluorophore-assisted cloning analysis
 IN Starr, Christopher M., Sonoma, CA, United States
 Klock, John C., Mill Valley, CA, United States
 Glyko, Inc., Novato, CA, United States (U.S. corporation)
 PA US 5258295 19931102
 PI US 1992-840739 19920225 (7)
 RLI Continuation of Ser. No. US 1991-643982, filed on 18 Jan 1991, now abandoned
 DT Utility
 FS Granted
 LN.CNT 796
 INCL INCLM: 435/172.300
 INCLS: 435/007.400; 536/001.110
 NCL NCLM: 435/006.000

NCLS: 435/007.400; 536/001.110
 IC [5]
 ICM: C12N015-10
 EXF 435/172.3; 935/9; 935/1; 935/6; 935/15; 935/19; 935/79; 935/80
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L6 ANSWER 31 OF 339 USPATFULL
 AN 93:91542 USPATFULL
 TI Vector containing DNA encoding mature human protein S
 IN Wydro, Robert, Framingham, MA, United States
 Cohen, Edward, Natick, MA, United States
 Dackowski, William, Hopkinton, MA, United States
 Stenflo, Johan, Malmö, Sweden
 Lundwall, Ake, Lund, Sweden
 Dahlback, Björn, Malmö, Sweden
 Genzyme Corporation, Cambridge, MA, United States (U.S. corporation)
 PA US 5258288 19931102
 PI US 1986-890401 19860725 (6)
 DT Utility
 FS Granted
 LN.CNT 529
 INCL INCLM: 435/069.600
 INCLS: 435/069.100; 435/172.300; 435/320.100; 435/235.100; 435/240.200; 536/023.500; 530/350.000; 935/019.000; 935/032.000; 935/041.000; 935/057.000; 935/062.000; 935/070.000
 NCL NCLM: 435/069.600
 NCLS: 435/069.100; 435/235.100; 435/320.100; 435/354.000; 530/350.000; 536/023.500
 IC [5]
 ICM: C12P021-02
 ICS: C12P019-34; C12N015-00; C12N007-00; C12N005-00; C07K003-00; C07H015-12
 EXF 435/68; 435/172.3; 435/320; 435/240; 435/69.1; 435/91; 435/235; 435/240.1; 435/320.1; 435/252.3; 530/350; 536/27
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L6 ANSWER 32 OF 339 USPATFULL
 AN 93:91541 USPATFULL
 TI DNA encoding and methods of production of insulin-like growth factor binding protein BP53
 IN Baxter, Robert C., Plebe, Australia
 Wood, William I., San Mateo, CA, United States
 Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
 PA Central Sydney Area Health Service, Camperdown, Australia (non-U.S. corporation)
 PI US 5258287 19931102
 AI US 1988-171623 19880322 (7)
 DT Utility
 FS Granted
 LN.CNT 1665
 INCL INCLM: 435/069.100
 INCLS: 536/023.500; 435/006.000; 435/069.800; 435/240.100; 435/240.200; 435/252.300; 435/254.110; 435/254.200; 435/320.100
 NCL NCLM: 435/069.100
 NCLS: 435/006.000; 435/069.800; 435/252.300; 435/254.110; 435/254.200; 435/320.100; 435/365.000; 435/369.000; 536/023.500
 IC [5]
 ICM: C12N005-10
 ICS: C12N001-15; C12N001-21; C12N015-12
 EXF 435/69.1; 435/6; 435/172.3; 435/69.8; 435/320.1; 435/254; 435/255; 435/256; 435/240.2; 435/240.1; 536/27
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 33 OF 339 USPATFULL
 AN 93:89649 USPATFULL
 TI Compositions of soluble complement receptor 1 (CRI) and a thrombolytic agent, and the methods of use thereof
 IN Fearon, Douglas T., Baltimore, MD, United States
 IN Klickstein, Lloyd B., Brookline, MA, United States
 IN Wong, Minnie W., Newton, MA, United States
 PA Carson, Gerald R., Wellesley, MA, United States
 PA Concino, Michael F., Newton, MA, United States
 PA Ip, Stephen H., Sudbury, MA, United States
 PA Makrides, Savvas, C., Bedford, MA, United States
 PA Marsh, Jr., Henry C., Reading, MA, United States
 PA The Johns Hopkins University, Baltimore, MD, United States (U.S. corporation)
 PI Brigham and Women's Hospital, Boston, MA, United States (U.S. corporation)
 PI T Cell Sciences, Inc., Cambridge, MA, United States (U.S. corporation)
 AI US 5256642 19931026
 RLI US 1990-588128 19900924 (7)
 Continuation-in-part of Ser. No. US 1989-412745, filed on 26 Sep 1989, now abandoned which is a continuation-in-part of Ser. No. US 1989-332865, filed on 3 Apr 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-176532, filed on 1 Apr 1988, now abandoned
 DT Utility
 FS Granted
 LN.CNT 4529
 INCL INCLM: 514/008.000
 INCL INCLS: 514/002.000; 424/094.630; 424/094.640; 435/215.000; 435/216.000; 530/350.000
 NCL NCLM: 514/008.000
 NCL INCLS: 424/094.630; 424/094.640; 435/215.000; 435/216.000; 514/002.000; 530/350.000
 IC [5]
 ICM: A61K037-02
 ICS: A61K037-547; C12N009-72; C07K013-00
 EXF 424/94.63; 424/94.64; 514/2; 514/8; 435/215; 435/216; 530/350
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 34 OF 339 USPATFULL
 AN 93:89568 USPATFULL
 TI Primitive cell colony stimulating factors and lymphohematopoietic progenitor cells
 IN Lawman, Michael J. P., Gainesville, FL, United States
 IN Ohmann, Helle B., Saskatchewan, Canada
 IN Attah-Poku, Samuel K., Saskatchewan, Canada
 IN Heise-Quattiere, Janette, Saskatchewan, Canada
 PA University of Saskatchewan, Saskatoon, Canada (non-U.S. corporation)
 PI US 5256580 19931026
 AI US 1991-677617 19910327 (7)
 RLI Continuation of Ser. No. US 1988-255088, filed on 7 Oct 1988, now abandoned
 DT Utility
 FS Granted
 LN.CNT 1557
 INCL INCLM: 435/240.200
 INCL INCLS: 435/240.210; 435/240.250
 NCL NCLM: 435/325.000
 NCL INCLS: 435/372.000
 IC [5]
 ICM: C12N005-00
 ICS: C12N005-02
 EXF 435/240.1; 435/240.2; 435/240.25; 435/240.3; 435/240.21; 435/240.25; 514/2; 424/930; 424/577

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 35 OF 339 USPATFULL
 AN 93:89566 USPATFULL
 TI Gene encoding plant asparagine synthetase
 IN Coruzzi, Gloria M., New York, NY, United States
 IN Tsai, Fong-Ying, New York, NY, United States
 PA The Trustees of Rockefeller University, New York, NY, United States (U.S. corporation)
 PI US 5256558 19931026
 AI US 1990-514816 19900426 (7)
 RLI Continuation-in-part of Ser. No. US 1989-347302, filed on 3 May 1989, now abandoned
 DT Utility
 FS Granted
 LN.CNT 1994
 INCL INCLM: 435/240.100
 INCL INCLS: 435/252.300; 435/320.100; 435/172.300; 435/252.330; 536/023.200; 536/024.100
 NCL NCLM: 435/252.330
 NCL INCLS: 435/252.300; 435/320.100; 536/023.200; 536/024.100
 IC [5]
 ICM: C12N005-10
 ICS: C12N001-19; C12N001-21; C12N015-52
 EXF 435/91; 435/172.3; 435/240.1; 435/252.3; 435/252.33; 435/254; 435/255; 435/183; 435/320.1; 536/27; 935/33; 935/34; 935/35
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 36 OF 339 USPATFULL
 AN 93:87584 USPATFULL
 TI Heterologous dominant conditional lethal gene which is a phosphonate monoester hydrolase and use thereof in plants
 IN Dotson, Stanton B., Fenton, MO, United States
 IN Kishore, Ganesh M., Chesterfield, MO, United States
 PA Monsanto Company, St. Louis, MO, United States (U.S. corporation)
 PI US 5254801 19931019
 AI US 1990-621670 19901203 (7)
 DT Utility
 FS Granted
 LN.CNT 2021
 INCL INCLM: 800/205.000
 INCL INCLS: 435/240.400; 435/172.300; 435/320.100; 435/069.100; 935/064.000; 935/067.000; 800/DIG.015
 NCL NCLM: 800/287.000
 NCL INCLS: 435/069.100; 435/320.100; 435/419.000; 536/023.200; 800/298.000; 800/303.000
 IC [5]
 ICM: A01H004-00
 ICS: C12N005-14; C12N015-82
 EXF 800/205; 800/DIG.15; 435/320.1; 435/172.3; 435/240.4; 435/69.1; 536/27; 935/64; 935/67
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 37 OF 339 USPATFULL
 AN 93:87456 USPATFULL
 TI Extracellular segments of human e immunoglobulin anchoring peptides and antibodies specific therefor
 IN Chang, Ise W., Houston, TX, United States
 PA Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
 PI US 5254671 19931019
 AI US 1992-973321 19921029 (7)
 RLI Continuation-in-part of Ser. No. US 1990-515604, filed on 27 Apr 1990, now abandoned
 DT Utility

FS Granted
LN.CNT 1331
INCL INCLM: 530/324.000
INCL: 530/350.000; 530/386.000; 536/023.530
NCL INCLM: 530/324.000
NCL: 530/350.000; 530/386.000; 536/023.530
IC [5]
ICM: C07K007-10
ICS: C12N015-13
EXF 536/23.23; 536/23.53; 530/324; 530/350; 530/386
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 38 OF 339 USPTAFULL
AN 93:87246 USPTAFULL
TI Nucleotide and amino acid sequences of protein MTP40 of M. tuberculosis and synthetic peptides derived therefrom
IN Patarkoy, Manuel E., Calle 135 No.15-40, Bogota, Colombia.
PI US 5254459 19931019
AI US 1992-940468 19920904 (7)
RLI Division of Ser. No. US 1990-572171, filed on 23 Aug 1990, now patented.
DT Utility
FS Granted
LN.CNT 535
INCL INCLM: 435/006.000
INCL: 435/732.000; 435/810.000; 435/863.000; 530/350.000; 530/326.000; 536/023.700; 536/024.320; 436/063.000; 436/808.000; 424/092.000
NCL INCLM: 435/006.000
NCL: 424/130.100; 424/248.100; 435/007.320; 435/810.000; 435/863.000; 436/063.000; 436/808.000; 530/326.000; 530/350.000; 536/023.700; 536/024.320
IC [5]
ICM: C12Q001-68
ICS: G01N033-569
EXF 530/350; 435/6; 435/7.32; 435/863; 435/810; 424/92; 436/63; 436/808
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 39 OF 339 USPTAFULL
AN 93:85275 USPTAFULL
TI .alpha.-l-anticithymotrypsin, analogues and methods of production
IN Rubin, Harvey, Philadelphia, PA, United States
PA Wang, Zhi M., Philadelphia, PA, United States
The Trustees of the University of Pennsylvania, Philadelphia, PA, United States (U.S. corporation)
PI US 5252725 19931012
AI US 1991-735335 19910724 (7)
RLI Division of Ser. No. US 1989-370704, filed on 23 Jun 1989, now patented.
DT Utility
FS Granted
LN.CNT 836
INCL INCLM: 536/023.500
INCL: 435/069.200; 435/172.100; 435/172.300; 435/213.000; 435/320.100
NCL INCLM: 536/023.500
NCL: 435/069.200; 435/213.000; 435/320.100
IC [5]
ICM: C07K003-00
ICS: C07K003-00; C12N015-09; A61K045-05
EXF 435/69.1; 435/69.2; 435/172.1; 435/172.3; 435/213; 435/320.1; 530/380; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 40 OF 339 USPTAFULL
AN 93:85267 USPTAFULL

TI Marek's disease herpesvirus DNA segments encoding glycoproteins, gp, gI and gE
IN Velicer, Leland F., East Lansing, MI, United States
Brunovskis, Peter, East Lansing, MI, United States
Cousens, Paul M., Dewitt, MI, United States
PA Board of Trustees operating Michigan State University, East Lansing, MI, United States (U.S. corporation)
PI US 5252717 19931012
AI US 1992-848697 19920309 (7)
RLI Division of Ser. No. US 1990-572711, filed on 24 Aug 1990, now patented.
DT Utility
FS Granted
LN.CNT 941
INCL INCLM: 530/395.000
NCL INCLM: 530/395.000
IC [5]
ICM: C07K013-00
EXF 530/395; 424/89
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 41 OF 339 USPTAFULL
AN 93:85266 USPTAFULL
TI Marek's disease herpesvirus DNA segments encoding glycoproteins, gp, gI and gE
IN Velicer, Leland F., East Lansing, MI, United States
Brunovskis, Peter, East Lansing, MI, United States
Cousens, Paul M., Dewitt, MI, United States
PA Board of Trustees operating Michigan State University, East Lansing, MI, United States (U.S. corporation)
PI US 5252716 19931012
AI US 1992-845957 19920304 (7)
RLI Division of Ser. No. US 1990-572711, filed on 24 Aug 1990, now patented.
DT Utility
FS Granted
LN.CNT 944
INCL INCLM: 530/395.000
NCL INCLM: 530/395.000
IC [5]
ICM: C07K013-00
EXF 530/395; 424/89
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 42 OF 339 USPTAFULL
AN 93:85018 USPTAFULL
TI Method of making antibodies to antigenic epitopes of IGE
present on B cells but not basophil cell surface or secreted, soluble IGE
IN Chang, Tse W., Houston, TX, United States
PA Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI US 5252467 19931012
AI US 1992-817916 19920106 (7)
RLI Division of Ser. No. US 1988-272243, filed on 16 Nov 1988, now patented.
Pat. No. US 5091313 which is a continuation-in-part of Ser. No. US 1988-229178, filed on 5 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 1988-226421, filed on 29 Jul 1988 which is a continuation-in-part of Ser. No. US 1987-140036, filed on 31 Dec 1987, now abandoned
DT Utility
FS Granted
LN.CNT 693
INCL INCLM: 435/070.210
INCL: 435/172.200; 435/240.270; 530/388.250; 530/389.300; 424/085.800;

NCL 514/014.000
NCLM: 435/070.210
NCLS: 424/153.100; 424/805.000; 424/810.000; 435/452.000; 514/014.000; 530/388.250; 530/388.730; 530/389.300; 530/862.000; 530/868.000

IC [5]
ICM: C12P021-08
ICS: C12N015-02; C12N005-12; C07K015-28
EXF 530/388.25; 530/389.3; 435/240.27; 435/172.2; 435/70.21; 514/14;
424/85.8
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 43 OF 339 USPTATFULL
AN 93:80738 USPTATFULL
TI Methods for inhibiting neoplastic cell proliferation using platelet factor 4
IN Twardzik, Daniel R., Bainbridge Island, WA, United States
PA Oncogen, Seattle, WA, United States (U.S. corporation)
PI US 5248665
AI US 1992-877341
RLI 19920429 (7)
Continuation of Ser. No. US 1988-159935, filed on 24 Feb 1988, now abandoned which is a continuation-in-part of Ser. No. US 1987-115139, filed on 30 Oct 1987, now abandoned which is a continuation-in-part of Ser. No. US 1987-20609, filed on 2 Mar 1987, now abandoned which is a continuation-in-part of Ser. No. US 1986-912407, filed on 26 Sep 1986, now patented, Pat. No. US 4737580 which is a division of Ser. No. US 1985-712302, filed on 15 Mar 1985, now patented, Pat. No. US 4645828, issued on 24 Feb 1987 which is a continuation-in-part of Ser. No. US 1984-592969, filed on 23 Mar 1984, now patented, Pat. No. US 4590003, issued on 20 May 1986

DT Utility
FS Granted
LN.CNT 1399
LN.CNT 1399
INCL INCLM: 514/012.000
INCLS: 514/002.000; 424/085.100; 530/324.000
NCL NCLM: 514/012.000
NCLS: 424/085.100; 514/002.000; 530/324.000
IC [5]
ICM: A61K037-02
EXF 514/2; 514/12; 530/324; 424/85.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 44 OF 339 USPTATFULL
AN 93:80681 USPTATFULL
TI Monoclonal antibodies and hybridomas specific for green-oat phytochrome
IN Cordonnier, Marie-Michele, Durham, NC, United States
Stewart, Lee, Athens, GA, United States
Stewart, Sandy, Durham, NC, United States
Montoya, Alice, Durham, NC, United States
PA Ciba-Geigy Corporation, Hawthorne, NY, United States (U.S. corporation)
PI US 5248607
AI US 1988-263618
RLI 19881027 (7)
Continuation of Ser. No. US 1988-263618, filed on 10 Dec 1988, now patented, Pat. No. US 4645828, issued on 24 Feb 1987 which is a continuation-in-part of Ser. No. US 1984-592969, filed on 23 Mar 1984, now patented, Pat. No. US 4590003, issued on 20 May 1986

DT Utility
FS Granted
LN.CNT 754
LN.CNT 754
INCL INCLM: 435/240.270
INCLS: 530/388.100; 530/391.100; 530/370.000; 435/172.200; 435/070.210
NCL NCLM: 435/341.000
NCLS: 435/070.210; 530/370.000; 530/388.100; 530/391.100
IC [5]
ICM: C12N005-12
ICS: C12P021-08; C07K015-28
EXF 530/387; 530/370; 530/388.1; 530/391.1; 435/240.27; 435/172.2; 435/70.21

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 45 OF 339 USPTATFULL
AN 93:80677 USPTATFULL
TI Superoxide dismutase
IN Marklund, Stefan, Ume ang., Sweden
Edlund, Thomas, Ume ang., Sweden
PA Synbiocom Aktiebolag, Umea, Sweden (non-U.S. corporation)
PI US 5248603
AI US 1992-897624
RLI 19920612 (7)
Continuation of Ser. No. US 1990-576114, filed on 27 Aug 1990, now patented, Pat. No. US 5130245 which is a continuation of Ser. No. US 1986-902596, filed on 2 Sep 1986, now abandoned

PRAI SE 1985-4027
DT Utility
FS Granted
LN.CNT 2242
LN.CNT 2242
INCL INCLM: 435/189.000
INCLS: 435/240.200; 435/320.100; 536/023.200
NCL NCLM: 435/189.000
NCLS: 435/320.100; 435/358.000; 536/023.200
IC [5]
ICM: C12N009-02
ICS: C12N015-53
EXF 435/189; 435/320.1; 435/240.2; 536/27; 536/23.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 46 OF 339 USPTATFULL
AN 93:78699 USPTATFULL
TI Bacillus thuringiensis isolate active against lepidopteran pests, and genes encoding novel lepidopteran-active toxins
IN Payne, Jewel, San Diego, CA, United States
Sick, August J., San Diego, CA, United States
PA Mycogen Corporation, San Diego, CA, United States (U.S. corporation)
PI US 5246852
AI US 1991-714413
RLI 19910612 (7)
Division of Ser. No. US 1989-371955, filed on 27 Jun 1989, now patented, Pat. No. US 5126133

DT Utility
FS Granted
LN.CNT 836
LN.CNT 836
INCL INCLM: 435/252.310
INCLS: 435/069.100; 435/172.300; 435/252.300; 435/252.340; 435/252.350; 435/320.100; 424/093.000A; 536/023.710
NCL NCLM: 435/252.310
NCLS: 424/093.200; 424/093.210; 435/069.100; 435/252.300; 435/252.350; 435/320.100; 536/023.710
IC [5]
ICM: C12N001-21
ICS: C12N015-32; C12N015-70; A01N063-00
EXF 435/69.1; 435/171.1; 435/91; 435/172.1; 435/172.3; 435/252.1; 435/252.3; 435/252.31; 435/252.34; 435/252.35; 435/320.1; 424/93; 935/6; 935/9; 935/22; 935/59; 935/61; 935/64; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 47 OF 339 USPTATFULL
AN 93:78691 USPTATFULL
TI Virulence associated proteins in Borrelia burgdorferi (BB)
IN Norris, Steven J., Houston, TX, United States
Barbour, Alan G., San Antonio, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5246844
AI US 1991-781355
19930921
19911022 (7)

DT Utility
FS Granted
LN.CNT 1705
INCL INCLM: 435/172.300
INCLM: 435/252.300; 435/320.100; 536/023.700; 536/024.320;
NCLM: 435/024.330
NCLM: 435/480.000
NCLM: 435/252.300; 435/252.330; 435/320.100; 435/476.000; 435/488.000;
NCLM: 536/023.700; 536/024.320; 536/024.330
IC [5]
ICM: C12N015-00
ICS: C12N015-03; C12N015-31
EXF 536/27; 435/6; 424/92
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 48 OF 339 USPATFULL
AN 93.76631 USPATFULL
TI Acute phase protein modulating endotoxic activity of
lipopolysaccharides, assay methods and polypeptides
IN Ulevitch, Richard, 1127 La Cuchara, Del Mar, CA, United States 92014
Tobias, Peter, 564 Arden Dr., Encinitas, CA, United States 92024
PI US 5245013 19930914
AI US 1989-367454 19890616 (7)
RLI Continuation-in-part of Ser. No. US 1986-67110, filed on 30 Dec 1986, now
abandoned which is a continuation-in-part of Ser. No. US 1985-728833,
filed on 30 Apr 1985, now abandoned

DT Utility
FS Granted
LN.CNT 2243
INCL INCLM: 530/380.000
INCLM: 530/350.000; 530/395.000
NCLM: 530/380.000
NCLM: 530/350.000; 530/395.000
IC [5]
ICM: C07K015-06
ICS: C07K015-14; A61K037-02
EXF 530/350; 530/380; 530/395
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 49 OF 339 USPATFULL
AN 93.76630 USPATFULL
TI Method to achieve solubilization of spider silk proteins
IN Lombardi, Stephen J., Brighton, MA, United States
Kaplan, David L., Stow, MA, United States
PA The United States of America as represented by the Secretary of the
Army, Washington, DC, United States (U.S. government)
PI US 5245012 19930914
AI US 1982-953323 19920929 (7)
RLI Continuation of Ser. No. US 1990-511114, filed on 19 Apr 1990, now
abandoned

DT Utility
FS Granted
LN.CNT 885
INCL INCLM: 530/353.000
INCLM: 530/412.000; 530/422.000; 530/425.000; 008/127.600; 008/128.100
NCLM: 530/353.000
NCLM: 008/127.600; 008/128.100; 530/412.000; 530/422.000; 530/425.000
IC [5]
ICM: C07K015-20
ICS: C07K003-00; C07K015-00; C07K015-08
EXF 530/353; 530/412; 530/422; 530/425; 008/127.6; 008/128.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L6 ANSWER 50 OF 339 USPATFULL

AN 93.76424 USPATFULL
TI DNA encoding novel tissue plasminogen activator derivatives having
kringles 1 and 2 deleted, vectors and host cells
IN Bang, Nils U., Indianapolis, IN, United States
Little, Sheila P., Indianapolis, IN, United States
Schoner, Brigitte E., Zionsville, IN, United States
Weigel, Barbara J., Indianapolis, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S.
corporation)
PI US 5244806 19930914
AI US 1990-614966 19901119 (7)
RLI Continuation of Ser. No. US 1989-348155, filed on 2 May 1989, now
abandoned which is a continuation of Ser. No. US 1986-889041, filed on
24 Jul 1986, now abandoned which is a continuation-in-part of Ser. No.
US 1985-769298, filed on 26 Aug 1985, now abandoned

DT Utility
FS Granted
LN.CNT 2723
INCL INCLM: 435/252.330
INCLM: 435/226.000; 435/240.200; 435/320.100; 536/023.200; 536/023.400;
NCLM: 536/023.500
NCLM: 435/252.330
NCLM: 435/226.000; 435/320.100; 435/359.000; 536/023.200; 536/023.400;
NCLM: 536/023.500
IC [5]
ICM: C12N009-64
ICS: C12N009-48; C12N005-00; C12N015-00
EXF 435/219; 435/212; 435/226; 435/320; 435/69.1; 435/172.3; 435/240.2;
435/252.33; 536/27; 536/23.2; 536/23.4; 536/23.5; 935/4; 935/10; 935/14;
935/29; 935/32; 935/70; 935/72
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his
(FILE 'HOME' ENTERED AT 12:23:05 ON 26 SEP 2002)
FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT
12:23:48 ON 26 SEP 2002
L1 41608 S ANTIBOD? AND LIBRAR?
L2 137092 S POLYCLONA?
L3 15758 S L2 AND L1
L4 9841 S L3 AND PHAGE?
L5 414 S L4 NOT PY=> 1994
L6 339 DUP REM L5 (75 DUPLICATES REMOVED)
=> s 16 and variabl? (a) region
L7 30 L6 AND VARIABLE? (A) REGION
=> d 17 1-30
L7 ANSWER 1 OF 30 MEDLINE
AN 94044806 MEDLINE
DN 94044806 PubMed ID: 8228264
TI Molecular selection of human antibodies with an unconventional
bacterial B cell antigen.
AU Sasano M; Burton D R; Silverman G J
CS Sam and Rose Stein Institute for Research on Aging, University of
California, San Diego, La Jolla 92093.
NC A100866 (NIAID)
AI34001 (NIAID)
SO JOURNAL OF IMMUNOLOGY, (1993 Nov 15) 151 (10) 5822-39.
CY Journal code: 2985117R. ISSN: 0022-1767.
United States

continuation-in-part of Ser. No. US 1987-111022, filed on 20 Oct 1987 which is a continuation-in-part of Ser. No. US 1986-922121, filed on 20 Oct 1986, now abandoned which is a continuation-in-part of Ser. No. US 1986-847931, filed on 7 Apr 1986, now abandoned which is a continuation-in-part of Ser. No. US 1985-725003, filed on 19 Apr 1985, now abandoned

DT Utility
FS Granted
LN.CNT 1446

INCL INCLM: 435/240.200
INCLS: 435/240.250; 530/399.000
NCL NCLM: 435/378.000
NCLS: 530/399.000

IC [5]

ICM: C12N005-08
ICS: C07K015-14

EXF 435/240.2; 435/240.21; 435/240.25; 514/2; 514/8; 514/25; 530/395; 530/399

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 7 OF 30 USPATFULL

AN 93:93905 USPATFULL

TI Antigenic epitopes present on membrane-bound but not secreted Ige
IN Chang, Tse-wen, Houston, TX, United States
PA Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI US 5260416 19931109
AI US 1990-468766 19900123 (7)

RLI Continuation-in-part of Ser. No. US 1989-369625, filed on 21 Jun 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-272243, filed on 16 Nov 1988, now patented, Pat. No. US 5091313 which is a continuation-in-part of Ser. No. US 1988-229178, filed on 5 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 1988-226421, filed on 29 Jul 1988 which is a continuation-in-part of Ser. No. US 1987-140036, filed on 31 Dec 1987, now abandoned

DT Utility
FS Granted
LN.CNT 859

INCL INCLM: 530/327.000
INCLS: 530/387.200; 530/387.300; 530/388.730; 530/862.000; 530/868.000; 424/085.800

NCL NCLM: 530/327.000

NCLS: 424/131.100; 424/139.100; 424/140.100; 424/153.100; 424/805.000; 424/810.000; 530/387.200; 530/387.300; 530/388.730; 530/862.000; 530/868.000

IC [5]

ICM: C07K007-08
ICS: C07K017-02

EXF 530/327; 530/388

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 8 OF 30 USPATFULL

AN 93:93713 USPATFULL

TI Methods for detection of human gamma, .gamma. T cell receptor

IN Brenner, Michael B., Ashland, MA, United States
Strominger, Jack L., Lexington, MA, United States
Seidman, John G., Milton, MA, United States
Ip, Stephen H., Framingham, MA, United States
Kranzel, Michael S., Newtonville, MA, United States
President & Fellows of Harvard College, Boston, MA, United States (U.S. corporation)
PA Dana Farber Cancer Institute & T Cell Diagnostics, Inc., Boston, MA, United States (U.S. corporation)

PI US 5260223 19931109
AI US 1988-187698 19880429 (7)

RLI Continuation-in-part of Ser. No. US 1987-115256, filed on 29 Oct 1987, now patented, Pat. No. US 5024940, issued on 18 Jun 1991 which is a continuation-in-part of Ser. No. US 1987-16252, filed on 19 Feb 1987 which is a continuation-in-part of Ser. No. US 1986-882100, filed on 3 Jul 1986, now abandoned

DT Utility
FS Granted
LN.CNT 1745

INCL INCLM: 436/501.000
INCLS: 435/007.100; 435/007.240; 435/172.200; 435/240.270; 436/506.000; 436/518.000; 436/548.000; 436/064.000; 530/387.900; 530/388.220; 530/388.750; 530/350.000; 536/023.500

NCL NCLM: 436/501.000

NCLS: 435/007.100; 435/007.240; 436/064.000; 436/506.000; 436/518.000; 436/548.000; 530/350.000; 530/387.900; 530/388.220; 530/388.750; 536/023.500

IC [5]

ICM: G01N033-566

EXF 435/7; 435/172.2; 435/240.27; 435/69.6; 435/7.1; 435/7.23; 436/501; 436/506; 436/518; 436/548; 436/811; 436/813; 436/64; 530/350; 530/387; 530/395; 530/828; 530/829; 935/110

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 9 OF 30 USPATFULL

AN 93:91541 USPATFULL

TI DNA encoding and methods of production of insulin-like growth factor binding protein BP53

IN Baxter, Robert C., Plebe, Australia
Wood, William I., San Mateo, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
Central Sydney Area Health Service, Camperdown, Australia (non-U.S. corporation)

PI US 5258287 19931102

AI US 1988-171623 19880322 (7)

DT Utility

FS Granted

LN.CNT 1665

INCL INCLM: 435/069.100

INCLS: 536/023.500; 435/006.000; 435/069.800; 435/240.100; 435/240.200; 435/252.300; 435/254.110; 435/254.200; 435/320.100

NCL NCLM: 435/069.100

NCLS: 435/006.000; 435/069.800; 435/252.300; 435/254.110; 435/254.200; 435/320.100; 435/365.000; 536/023.500

IC [5]

ICM: C12N005-10

ICS: C12N001-15; C12N001-21; C12N015-12

EXF 435/69.1; 435/6; 435/172.3; 435/69.8; 435/320.1; 435/254; 435/255; 435/256; 435/240.2; 435/240.1; 536/27

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 10 OF 30 USPATFULL

AN 93:87456 USPATFULL

TI Extracellular segments of human e immunoglobulin anchoring peptides and antibodies specific thereof

IN Chang, Tse W., Houston, TX, United States
Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI US 5254671 19931019

AI US 1992-973321 19921029 (7)

RLI Continuation-in-part of Ser. No. US 1990-515604, filed on 27 Apr 1990, now abandoned

DT Utility

FS Granted

LN.CNT 1331

DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Abridged Index Medicus Journals; Priority Journals
OS GENBANK-L19902; GENBANK-L19903; GENBANK-L19904; GENBANK-L19905;
GENBANK-L19906; GENBANK-L19907; GENBANK-L19908; GENBANK-L19909;
GENBANK-L19910; GENBANK-L19911; GENBANK-L19912; GENBANK-L19913;
GENBANK-L19914; GENBANK-L19915; GENBANK-L19916; GENBANK-L19917;
GENBANK-L19918; GENBANK-L19919; GENBANK-L19920
199112

EM Entered STN: 19940117
ED Last Updated on STN: 19940117
Entered Medline: 19931210

L7 ANSWER 2 OF 30 MEDLINE
AN 90005436 MEDLINE
DN 90005436 PubMed ID: 2477243
TI Molecular cloning of the primary Igh repertoire: a quantitative analysis
of VH gene usage in adult mice.

AU Sheehan K M; Brodeur P H
CS Immunology Program, Sackler School of Graduate Biomedical Sciences,
Boston, MA.

NC AI-07-77-07 (NIAID)
P01-AI 23495 (NIGMS)
R01-GM 36064

SO EMBO JOURNAL, (1989 Aug) 8 (8) 2313-20.
Journal code: 8208664. ISSN: 0261-4189.

CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals

EM 198911
ED Entered STN: 19900328
Last Updated on STN: 19970203
Entered Medline: 19891109

L7 ANSWER 3 OF 30 USPATFULL

AN 93:107133 USPATFULL
TI DNA sequences encoding vascular cell adhesion molecules (VCAMS)
IN Hession, Catherine A.; South Weymouth, MA, United States
Lobb, Roy R.; Westwood, MA, United States
Goelz, Susan E.; Winchester, MA, United States
Osborn, Laurelee, Brighton, MA, United States
Benjamin, Christopher D.; Beverly, MA, United States
Rosa, Margaret D.; Winchester, MA, United States
Biogen, Inc.; Cambridge, MA, United States (U.S. corporation)
US 5272263 19931221
US 1989-452675 19891218 (7)

PA Continuation-in-part of Ser. No. US 1989-359516, filed on 1 Jun 1989,
now abandoned which is a continuation-in-part of Ser. No. US
1989-345151, filed on 28 Apr 1989

DT Utility
FS Granted

INCL INCLM: 536/023.500

INCL INCLM: 536/023.500
INCLM: 530/380.000; 435/069.600; 435/320.100

NCL NCLM: 536/023.500
NCLM: 435/069.600; 435/320.100; 530/380.000

IC [5]
ICM: C07K013-00

EXF ICS: C12N015-00; C12P021-06
435/69.1; 435/69.9; 435/320.1; 530/380; 536/27

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 30 USPATFULL

AN 93:102708 USPATFULL
TI Mammalian adipocyte protein p154, nucleic acids coding therefor and uses
thereof.
IN Serrero, Ginette, Lake Placid, NY, United States
PA W. Alton Jones Cell Science Center, Inc., Lake Placid, NY, United States
(U.S. corporation)
PI US 5268295 19931207
AI US 1991-708038 19910531 (7)

DT Utility
FS Granted

INCL INCLM: 435/252.300
INCLM: 435/069.100; 435/070.100; 435/070.300; 435/071.100; 435/172.300;
435/240.200; 435/320.100; 536/023.500; 935/011.000; 935/027.000;
935/056.000; 935/066.000

NCL NCLM: 435/252.300
NCLM: 435/069.100; 435/070.100; 435/070.300; 435/071.100; 435/320.100;
536/023.500

IC [5]
ICM: C12N015-12

EXF ICS: C12N015-63
536/27; 536/23.5; 435/69.1; 435/70.1; 435/70.3; 435/71.1; 435/172.3;
435/240.2; 435/252.3; 435/320.1; 935/8; 935/11; 935/12; 935/24; 935/27;
935/56; 935/66

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 5 OF 30 USPATFULL
AN 93:98498 USPATFULL
TI Platelet cell adhesion molecule and variants thereof
IN Newman, Peter J.; Shorewood, WI, United States
PA The Blood Center of Southeastern Wisconsin, Inc., Milwaukee, WI, United
States (U.S. corporation)
PI US 5264554 19931123
AI US 1990-466140 19900119 (7)

DT Utility
FS Granted

INCL INCLM: 530/387.100
INCLM: 530/395.000; 530/350.000; 530/324.000; 435/069.100; 424/085.800

NCL NCLM: 530/387.100
NCLM: 435/069.100; 530/324.000; 530/350.000; 530/387.100; 530/395.000;
536/023.500

IC [5]
ICM: C07K013-00

EXF ICS: C07K009-00; C07K015-14; A61K039-00
530/387; 530/388; 530/395; 530/330; 530/329; 530/328; 530/327;
530/326; 530/325; 530/324; 530/350; 530/387.1; 514/8; 514/12; 435/69.1;
424/85.8

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 6 OF 30 USPATFULL
AN 93:96039 USPATFULL

TI Method for obtaining bone marrow free of tumor cells using transforming
growth factor .beta.3
IN Iwata, Kenneth K.; Westbury, NY, United States
Faulkes, J. Gordon, Huntington, NY, United States
Dijke, Peter T.; Port Washington, NY, United States
Haley, John D.; Great Neck, NY, United States
Oncogene Science, Inc., Uniondale, NY, United States (U.S. corporation)

PI US 5262319 19931116
AI US 1990-543341 19900625 (7)

RLI Continuation-in-part of Ser. No. US 1989-353410, filed on 17 May 1989,
now abandoned which is a continuation-in-part of Ser. No. US
1988-183824, filed on 20 Apr 1988, now abandoned which is a

INCL INCLM: 530/324.000
INCL: 530/350.000; 530/386.000; 536/023.530
NCL NCLM: 530/324.000
NCL: 530/350.000; 530/386.000; 536/023.530
IC [5]
ICM: C07K007-10
ICS: C12N015-13
EXF 536/23.23; 536/23.53; 530/324; 530/350; 530/386
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 11 OF 30 USPATFULL
AN 93:76410 USPATFULL
TI Expression of recombinant glycoprotein B from herpes simplex virus
IN Burke, Rae L., San Francisco, CA, United States
PA Pachl, Carol, Oakland, CA, United States
PI Valenzuela, Pablo D. T., San Francisco, CA, United States
RI Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
US 5244792 19930914
AI US 1990-587179 19900920 (7)
RLI Continuation of Ser. No. US 1986-921730, filed on 20 Oct 1986, now abandoned which is a continuation-in-part of Ser. No. US 1984-597784, filed on 6 Apr 1984, now abandoned
DT utility
FS Granted
LN.CNT 1639
INCL INCLM: 435/069.300
INCL: 435/240.200; 435/320.100; 435/069.100; 435/070.300; 435/071.100; 435/172.300; 435/254.200; 536/023.720; 935/012.000; 935/069.000; 935/070.000; 424/089.000
NCL NCLM: 435/069.300
NCL: 424/186.100; 424/231.100; 435/069.100; 435/070.300; 435/071.100; 435/254.200; 435/320.100; 435/362.000; 435/364.000; 435/365.000; 536/023.720
IC [5]
ICM: C12P021-06
ICS: C12N005-00; C12N015-00; C07H021-00
EXF 435/69.1; 435/69.3; 435/240.2; 435/320.01; 435/255; 435/70.1; 435/70.3; 435/172.3; 424/88; 935/12; 935/69; 935/70; 536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 12 OF 30 USPATFULL
AN 93:61035 USPATFULL
TI DNA encoding murine-human chimeric antibodies specific for antigenic epitopes of IgE present on the extracellular segment of the membrane domain of membrane-bound IgE
IN Chang, Tse W., Houston, TX, United States
PA Tanox Biosystems, Inc., Houston, TX, United States (U.S. corporation)
PI US 5231026 19930727
AI US 1992-618781 19920106 (7)
RLI Division of Ser. No. US 1988-272243, filed on 16 Nov 1988, now patented, Pat. No. US 5091313 which is a continuation-in-part of Ser. No. US 1988-229178, filed on 5 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 1988-226421, filed on 29 Jul 1988, now abandoned which is a continuation-in-part of Ser. No. US 1987-140036, filed on 31 Dec 1987, now abandoned
DT utility
FS Granted
LN.CNT 667
INCL INCLM: 435/252.300
INCL: 435/172.300; 435/320.100; 435/240.270; 435/240.200; 530/387.300; 530/388.250; 536/023.530
NCL NCLM: 435/252.300
NCL: 435/320.100; 435/328.000; 530/387.300; 530/388.250; 536/023.530
IC [5]

ICM: C12N001-20
ICS: C12N005-10; C12N015-00; C07H015-12
EXF 536/27; 536/172.3; 536/23.53; 435/252.3; 435/252.33; 435/320.1; 435/255; 435/240.29; 435/240.2; 530/388.25; 530/387.3
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 13 OF 30 USPATFULL
AN 93:54852 USPATFULL
TI Lymphocyte homing receptor/immunoglobulin fusion proteins
IN Capon, Daniel J., San Mateo, CA, United States
PA Lasky, Laurence A., Sausalito, CA, United States
PI Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
US 5225538 19930706
AI US 1991-808122 19911216 (7)
RLI Division of Ser. No. US 1989-440625, filed on 22 Nov 1989, now patented, Pat. No. US 5116984 which is a continuation of Ser. No. US 1989-315015, filed on 23 Feb 1989, now patented, Pat. No. US 5098833
DT utility
FS Granted
LN.CNT 2558
INCL INCLM: 530/387.300
INCL: 435/069.700; 530/388.730
NCL NCLM: 530/387.300
NCL: 424/134.100; 435/069.700; 530/388.730
IC [5]
ICM: C07K013-00
ICS: C17N015-62
EXF 435/69.7; 530/387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 14 OF 30 USPATFULL
AN 93:52487 USPATFULL
TI Directed evolution of novel binding proteins
IN Ladher, Robert C., Ijamsville, MD, United States
Guterman, Sonia K., Belmont, MA, United States
Roberts, Bruce L., Milford, MA, United States
Markland, William, Milford, MA, United States
Ley, Arthur C., Newton, MA, United States
PA Kent, Rachel B., Boxborough, MA, United States
Protein Engineering Corp., Cambridge, MA, United States (U.S. corporation)
PI US 5223409 19930629
AI US 1991-664989 19910301 (7)
RLI Continuation-in-part of Ser. No. US 1990-487063, filed on 2 Mar 1990, now abandoned and a continuation-in-part of Ser. No. US 1988-240160, filed on 2 Sep 1988, now abandoned
DT utility
FS Granted
LN.CNT 15410
INCL INCLM: 435/069.700
INCL: 435/069.100; 435/172.300; 435/252.300; 435/320.100; 530/380.300; 530/387.500
NCL NCLM: 435/069.700
NCL: 435/005.000; 435/069.100; 435/252.300; 435/320.100; 435/472.000; 530/387.500
IC [5]
ICM: C12N015-09
ICS: C12N015-62; C12N015-63
EXF 435/69.1; 435/172.3; 435/252.3; 435/320.1; 530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 15 OF 30 USPATFULL
AN 93:48655 USPATFULL

TI Recombinant antibodies and methods for their production in which surface residues are altered to cysteine residues for attachment of effector or receptor molecules

IN Bodmer, Mark W., Oxfordshire, United Kingdom
Adair, John R., High Wycombe, United Kingdom
Whittle, Nigel R., Surrey, United Kingdom
Lyons, Alan H., Maidenhead, United Kingdom
Owens, Raymond J., Henley-on-Thames, United Kingdom
Celltech Limited, Berkshire, United Kingdom (non-U.S. corporation)
US 5219996 19930615
WO 8901782 19890309
US 1989-353634 19880905
WO 1988-CB729 19880905

PA 19890703 PCT 371 date
19890703 PCT 102(e) date
19890703

PI CB 1987-20833 19870904

DT Utility

FS Granted

LN.CNT 578

INCL INCLM: 530/387.300
INCLS: 530/387.100; 530/391.100; 530/391.500; 424/085.800; 424/085.910; 435/069.600; 435/070.210; 435/172.200; 435/172.300; 435/240.270; 435/320.100
NCLM: 530/387.300
NCLS: 424/133.100; 424/178.100; 424/801.000; 435/069.600; 435/070.210; 435/091.410; 435/320.100; 435/466.000; 530/387.100; 530/388.850; 530/391.100; 530/391.500; 530/867.000; 536/023.530

IC [5]
ICM: C07K015-28
ICS: A61K039-395; C12P021-08
424/85.8; 424/85.91; 435/69.1; 435/69.6; 435/70.21; 435/172.1; 435/172.2; 435/172.3; 435/240.27; 435/320.1; 530/387.389; 530/387.1; 530/387.3; 530/391.5; 530/391.1

EXP 435/172.2; 435/172.3; 435/240.27; 435/320.1; 530/387.389; 530/387.1; 530/387.3; 530/391.5; 530/391.1

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 16 OF 30 USPATFULL

AN 93:39900 USPATFULL

TI Genetic material encoding new insulin-like growth factor binding protein

IN Kiefer, Michael C., Clayton, CA, United States

PA Masiazz, Frank R., San Francisco, CA, United States

PI Chiron Corporation, Emeryville, CA, United States (U.S. corporation)
US 5212074 19930518
US 1990-576629 19900831 (7)
US 1990-576629 19900831 (7)

AI Division of Ser. No. US 1990-574613, filed on 28 Aug 1990, now abandoned

DT Utility

FS Granted

LN.CNT 1731

INCL INCLM: 435/069.600
INCLS: 435/069.100; 435/252.300; 435/240.100; 435/243.000; 435/254.000; 536/023.500; 935/009.000; 935/011.000; 935/066.000; 530/395.000
NCLM: 435/069.600
NCLS: 435/069.100; 435/243.000; 435/252.300; 435/361.000; 530/395.000; 536/023.500

IC [5]
ICM: C12P021-02
ICS: C07H021-04; C12N001-00
514/44; 530/303; 530/399; 435/69.1; 435/70.1; 435/71.1; 435/252.3; 435/252.33; 435/255; 435/240.2; 435/69.5; 435/240.1; 435/240.2; 435/240.4; 435/254; 435/255; 435/243; 435/69.6; 935/13; 935/9; 800/2; 536/27

EXP 435/252.33; 435/255; 435/240.2; 435/69.5; 435/240.1; 435/240.2; 435/240.4; 435/254; 435/255; 435/243; 435/69.6; 935/13; 935/9; 800/2; 536/27

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 17 OF 30 USPATFULL

AN 93:22595 USPATFULL

TI Characterization of platelet aggregation disorders

IN Ginsberg, Mark H., San Diego, CA, United States

PA The Scripps Research Institute, La Jolla, CA, United States (U.S. corporation)

PI US 5196309 19930323
US 1990-614723 19901115 (7)

AI Utility

DT Utility

FS Granted

LN.CNT 1855

INCL INCLM: 435/007.210
INCLS: 435/007.240; 436/503.000; 436/548.000
NCLM: 435/007.210
NCLS: 435/007.240; 436/503.000; 436/548.000

IC [5]
ICM: G01N033-567
ICS: G01N033-577
435/7.21; 435/7.24; 436/503; 436/548; 436/811; 935/110

EXP 435/7.21; 435/7.24; 436/503; 436/548; 436/811; 935/110

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 18 OF 30 USPATFULL

AN 93:10435 USPATFULL

TI Human gamma., .delta.T cell antigen receptor polypeptides and nucleic acids

IN Brenner, Michael B., Sherborn, MA, United States
Seidman, Jonathan, Milton, MA, United States
Strominger, Jack L., Lexington, MA, United States
Ip, Stephen H., Sudbury, MA, United States
Kragel, Michael S., Chapel Hill, NC, United States
Band, Hamid, Boston, MA, United States
T Cell Sciences, Inc., Cambridge, MA, United States (U.S. corporation)
Dana Farber Cancer Institute, Boston, MA, United States (U.S. corporation)

PA President & Fellows of Harvard College, Boston, MA, United States (U.S. corporation)

PI US 5185250 19930209
US 1989-237661 19890113 (7)

AI Continuation-in-part of Ser. No. US 1988-187698, filed on 29 Apr 1988

RLI which is a continuation-in-part of Ser. No. US 5024940 which is a Oct 1987, now patented, Pat. No. US 5024940 which is a continuation-in-part of Ser. No. US 1987-16252, filed on 19 Feb 1987 which is a continuation-in-part of Ser. No. US 1986-882100, filed on 3 Jul 1986, now abandoned

DT Utility

FS Granted

LN.CNT 5332

INCL INCLM: 435/069.300
INCLS: 435/069.100; 435/007.240; 435/172.200; 435/240.270; 530/350.000; 530/387.900; 530/388.220; 530/388.750; 536/023.500
NCLM: 435/069.300
NCLS: 435/007.240; 435/069.100; 530/350.000; 530/387.900; 530/388.220; 530/388.750; 536/023.500

IC [5]
ICM: C12P021-06
ICS: C12N005-02; A61K035-14; C07H015-12
435/7; 435/69.1; 435/172.2; 435/172.3; 435/68.1; 435/70; 435/6; 435/240.27; 435/69.3; 536/27; 530/387; 530/359

EXP 435/7; 435/69.1; 435/172.2; 435/172.3; 435/68.1; 435/70; 435/6; 435/240.27; 435/69.3; 536/27; 530/387; 530/359

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 19 OF 30 USPATFULL

AN 93:5468 USPATFULL

TI Versican core protein, nucleic acid sequences encoding the same, nucleic acid probes, anti-versican antibodies, and methods of detecting the same

IN PA Ruoslahti, Erkki I., Rancho Santa Fe, CA, United States
La Jolla Cancer Research Foundation, La Jolla, CA, United States (U.S. corporation)

PI US 5180808 19930119
AI US 1989-441179 19891127 (7)
DT Utility
FS Granted
LN.CNT 559
INCL INCLM: 530/350.000
INCLS: 530/387.900; 530/388.200; 530/389.100; 536/023.500
NCL NCLM: 530/350.000
NCLS: 530/387.900; 530/388.200; 530/389.100; 536/023.500
IC [5]
ICM: C07K003-00
ICS: C07H015-12
EXF 436/561; 436/23; 436/503; 436/519; 536/27; 530/350; 530/387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 20 OF 30 USPATFULL
AN 92:84786 USPATFULL
TI Method of producing secreted receptor analogs and biologically active peptide dimers
IN Sledziewski, Andrzej Z., Seattle, WA, United States
Bell, Lillian A., Seattle, WA, United States
Kindsvogel, Wayne R., Seattle, WA, United States (U.S. corporation)
PA ZymoGenetics, Inc., Seattle, WA, United States (U.S. corporation)
PI US 5155027 19921013
AI US 1989-347291 19890502 (7)
PRAI EP 1989-100787 19890118
DT Utility
FS Granted
LN.CNT 2238
INCL INCLM: 435/069.700
INCLS: 435/172.300; 530/387.300; 530/350.000; 530/388.220
NCL NCLM: 435/069.700
NCLS: 435/483.000; 530/350.000; 530/388.220; 530/389.300
IC [5]
ICM: C12N015-62
EXF 435/68; 435/70; 435/235; 435/320; 435/243; 435/253; 435/272; 435/240.27; 435/240.2; 435/240.1; 435/69.7; 435/172.3; 530/356; 530/387
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 21 OF 30 USPATFULL
AN 92:72459 USPATFULL
TI Method and means for extending the host range of insecticidal proteins
IN Sivasubramanian, Natarajan, Riverside, CA, United States
Federici, Brian A., Riverside, CA, United States
PA The Regents of the University of California, Oakland, CA, United States (U.S. corporation)
PI US 5143905 19920901
AI US 1990-518575 19900503 (7)
DT Utility
FS Granted
LN.CNT 1364
INCL INCLM: 514/021.000
INCLS: 514/008.000; 514/012.000; 530/350.000; 530/409.000; 424/405.000;
NCL NCLM: 435/069.700
NCLS: 514/021.000
NCLS: 424/405.000; 435/069.700; 514/008.000; 514/012.000; 530/350.000;
530/409.000
IC [5]
ICM: C07K003-08
ICS: A61K037-00; A61K039-07; A61K039-12
EXF 530/350; 530/409; 514/21; 514/8; 514/12; 424/405

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 22 OF 30 USPATFULL
AN 92:70238 USPATFULL
TI Marker for early detection of human hydatidiform moles and choriocarcinomas
IN Chou, Janice, Potomac, MD, United States
PA The United States of America as represented by the Department of Health and Human Services, Washington, DC, United States (U.S. government)
PI US 5141849 19920825
AI US 1990-536101 19900608 (7)
DT Utility
FS Granted
LN.CNT 669
INCL INCLM: 435/006.000
INCLS: 435/007.100; 435/810.000; 536/026.000; 536/027.000; 536/028.000;
536/029.000; 530/326.000; 530/328.000; 530/387.900; 530/388.200;
530/388.850; 530/389.100; 530/389.700; 935/077.000; 935/078.000;
436/501.000; 436/094.000
NCL NCLM: 435/006.000
NCLS: 435/007.100; 435/810.000; 436/501.000; 530/326.000; 530/328.000;
530/387.900; 530/388.200; 530/388.850; 530/389.100; 530/389.700;
536/023.500; 536/024.310
IC [5]
ICM: C12Q001-68
ICS: G01N033-53; A61K037-02; C07H015-12
EXF 536/26; 536/27; 536/28; 435/6; 435/7.1; 435/7.23; 530/328; 530/326;
530/387; 935/77; 935/78
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 23 OF 30 USPATFULL
AN 92:42890 USPATFULL
TI Hybrid immunoglobulins
IN Capon, Daniel J., San Mateo, CA, United States
Lasky, Laurence A., Sausalito, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 5116964 19920526
AI US 1989-440625 19891122 (7)
RLI Continuation-in-part of Ser. No. US 1989-315015, filed on 23 Feb 1989
DT Utility
FS Granted
LN.CNT 2533
INCL INCLM: 536/027.000
INCLS: 435/069.700; 435/252.300; 435/320.110; 530/350.000
NCL NCLM: 536/023.500
NCLS: 424/134.100; 435/069.700; 435/252.300; 435/320.100; 530/350.000;
530/387.300; 536/023.510; 536/023.530
IC [5]
ICM: C07H021-04
ICS: C12N015-62; C12P021-02
EXF 435/69.7; 435/172.3; 435/252.3; 435/320; 436/512; 530/350; 530/387;
536/27
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 24 OF 30 USPATFULL
AN 92:36281 USPATFULL
TI Derivatives of soluble T-4
IN Maddon, Paul J., New York, NY, United States
Axel, Richard, New York, NY, United States
Sweet, Raymond W., Bala Cynwyd, PA, United States
PA Athos, James, Ann Arbor, MI, United States
The Trustees of Columbia University in the City of New York, New York, NY, United States (U.S. corporation)

Smithline Beckman Corporation, Philadelphia, PA, United States (U.S. corporation)
 PI US 5110906 19920505
 AI US 1988-160348 19880224 (7)
 RLI Continuation-in-part of Ser. No. US 1987-114244, filed on 23 Oct 1987 which is a continuation-in-part of Ser. No. US 1986-89587, filed on 21 Aug 1986, now abandoned
 DT Utility
 FS Granted
 LN.CNT 2771
 INCL INCLM: 430/350.000
 INCLS: 435/005.000; 435/974.000; 530/395.000; 530/829.000; 930/221.000
 NCL NCLM: 530/350.000
 NCLS: 435/005.000; 435/974.000; 530/395.000; 530/821.000; 930/221.000
 IC [5]
 ICM: C07K013-00
 EXF 530/387; 530/395; 530/350; 530/829; 930/221; 435/5; 435/974
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L7 ANSWER 25 OF 30 USPATFULL
 AN 92:3765 USPATFULL
 TI Interleukin-1 receptors
 IN Dower, Steven K., Redmond, WA, United States
 March, Carl J., Seattle, WA, United States
 Sims, John E., Seattle, WA, United States
 Urdal, David L., Seattle, WA, United States
 Immunex Corporation, Seattle, WA, United States (U.S. corporation)
 PA US 5081228 19920114
 PI US 1988-258756 19881013 (7)
 AI US 1988-258756 19881013 (7)
 RLI Continuation-in-part of Ser. No. US 1988-160550, filed on 25 Feb 1988, now patented, Pat. No. US 4968607 which is a continuation-in-part of Ser. No. US 1987-125627, filed on 25 Nov 1987, now abandoned
 DT Utility
 FS Granted
 LN.CNT 1540
 INCL INCLM: 530/035.100
 INCLS: 530/350.000; 530/395.000; 530/820.000; 435/069.500; 435/069.100; 424/085.100; 424/085.200; 514/002.000; 514/008.000
 NCL NCLM: 530/351.000
 NCLS: 424/085.100; 424/085.200; 435/069.100; 435/069.500; 514/002.000; 514/008.000; 530/350.000; 530/395.000; 530/820.000
 IC [5]
 ICM: C07K013-00
 EXF 530/351; 530/350; 530/395; 530/820; 435/68; 435/70; 514/2; 514/8; 424/85.1; 424/85.2
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L7 ANSWER 26 OF 30 USPATFULL
 AN 91:42649 USPATFULL
 TI Synovial phospholipases
 IN Johnson, Lorin K., Pleasanton, CA, United States
 Sellhauer, Jeffrey J., Milpitas, CA, United States
 Pruzanski, Waldemar, Ontario, Canada
 Vadas, Peter, Ontario, Canada
 Biotechnology Research Partners, Ltd., Ontario, CA, United States (U.S. corporation)
 PA The University of Toronto Innovations Foundation, Ontario, Canada (non-U.S. corporation)
 PI US 5019508 19910528
 AI US 1988-215726 19880706 (7)
 RLI Continuation-in-part of Ser. No. US 1987-89883, filed on 27 Aug 1987, now abandoned
 DT Utility

FS Granted
 LN.CNT 1397
 INCL INCLM: 435/198.000
 INCLS: 435/172.100; 435/320.100; 435/252.300; 536/027.000; 935/014.000
 NCL NCLM: 435/198.000
 NCLS: 435/252.300; 435/320.100; 536/023.200; 536/023.500
 IC [5]
 ICM: C12N009-20
 EXF 435/172.3; 435/198; 435/320; 435/240.2; 435/252.3; 435/235; 435/255; 935/14; 935/28; 935/29; 935/31; 935/56; 935/58; 935/69; 935/71; 935/72; 536/27
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L7 ANSWER 27 OF 30 USPATFULL
 AN 90:85544 USPATFULL
 TI Interleukin-1 receptors
 IN Dower, Steven K., Redmond, WA, United States
 March, Carl J., Seattle, WA, United States
 Sims, John E., Seattle, WA, United States
 Urdal, David L., Seattle, WA, United States
 Immunex Corporation, Seattle, WA, United States (U.S. corporation)
 PA US 4968607 19901106
 PI US 1988-160550 19880225 (7)
 AI US 1988-160550 19880225 (7)
 RLI Continuation-in-part of Ser. No. US 1987-125627, filed on 25 Nov 1987
 DT Utility
 FS Granted
 LN.CNT 1513
 INCL INCLM: 435/069.100
 INCLS: 536/027.000; 435/320.000; 435/235.000; 435/240.100; 435/252.800; 435/255.000; 330/387.000; 330/399.000
 NCL NCLM: 435/069.100
 NCLS: 435/235.100; 435/252.800; 530/388.220; 530/399.000; 536/023.500; 536/023.510; 536/024.310
 IC [5]
 ICM: C12N015-00
 EXF 435/252.8; 435/255; 530/387; 530/399
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L7 ANSWER 28 OF 30 USPATFULL
 AN 90:76640 USPATFULL
 TI Compositions and methods for the synthesis and assay of a mammalian enkephalinase
 IN Malfiroy-Camine, Bernard, San Bruno, CA, United States
 Schofield, Peter R., San Francisco, CA, United States
 Genentech, Inc., So. San Francisco, CA, United States (U.S. corporation)
 PA US 4960700 19901002
 PI US 1987-2478 19870112 (7)
 RLI Continuation-in-part of Ser. No. US 1986-946566, filed on 24 Dec 1986
 DT Utility
 FS Granted
 LN.CNT 1420
 INCL INCLM: 435/172.300
 INCLS: 435/212.000; 435/219.000; 435/240.200; 435/252.330; 435/071.100; 435/091.000; 435/172.100; 435/172.300; 435/320.000; 536/027.000; 530/350.000; 935/018.000; 935/031.000; 935/041.000; 935/058.000; 935/070.000; 935/073.000; 935/082.000
 NCL NCLM: 435/219.000
 NCLS: 435/212.000; 435/252.330; 435/358.000; 435/369.000
 IC [5]
 ICM: C12N009-48
 ICS: C12N009-50; C12N005-00; C12N001-22; C12N015-00; C12N001-00;

EXF C12P021-04; C12P019-34; C07H015-12; C07K013-00
 435/68; 435/70; 435/91; 435/172.1; 435/172.3; 435/219; 435/212; 530/350;
 935/19; 935/34; 935/70
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 29 OF 30 USPATFULL
 AN 89:98909 USPATFULL
 TI Diagnostic reagents based on unique sequences within the
 variable region of the T cell receptor and uses
 thereof
 IN Hood, Leroy E., Pasadena, CA, United States
 Weissman, Irving L., Stanford, CA, United States
 McGrath, Michael S., Menlo Park, CA, United States
 PA California Institute of Technology, Pasadena, CA, United States (U.S.
 corporation)
 PI US 4886743 19891212
 AI US 1985-726502 19850424 (6)
 DT Utility
 FS Granted
 LN.CNT 1777
 INCL INCLM: 435/005.000
 INCLS: 435/006.000; 435/007.000; 435/029.000; 530/387.000; 530/326.000;
 935/078.000; 935/104.000; 935/011.000; 935/012.000; 436/548.000;
 436/813.000; 436/536.000; 436/052.000; 436/063.000; 436/506.000;
 436/508.000; 436/509.000
 NCLM: 435/005.000
 NCLS: 435/006.000; 435/007.220; 435/007.230; 435/007.240; 435/029.000;
 435/188.000; 435/974.000; 436/052.000; 436/063.000; 436/506.000;
 436/508.000; 436/509.000; 436/536.000; 436/548.000; 436/813.000;
 530/326.000; 530/387.900; 530/388.220; 530/388.750; 530/388.900;
 530/389.100; 530/389.600; 530/389.800; 530/391.300; 536/024.300
 IC [4]
 ICM: C12Q001-68
 ICS: G01N033-53; G01N033-569; C07K007-10
 435/5-7; 435/29; 436/810; 436/501; 436/503; 436/504; 436/506; 436/508;
 436/509; 436/518; 436/536; 436/548; 436/813; 436/820; 436/52; 436/63;
 935/11; 935/12; 935/78; 935/25; 935/80; 935/81; 935/104; 530/326;
 530/387; 530/388; 536/27
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 30 OF 30 USPATFULL
 AN 89:23522 USPATFULL
 TI Recombinant immunoglobulin preparations
 IN Cabilly, Shmuel, Monrovia, CA, United States
 Heyneker, Herbert L., Burlingame, CA, United States
 Holmes, William E., Pacifica, CA, United States
 Riggs, Arthur D., La Verne, CA, United States
 PA Wetzel, Ronald B., San Francisco, CA, United States
 Genentech, Inc., South San Francisco, CA, United States (U.S.
 corporation)
 PI US 4816567 19890328
 AI US 1983-483457 19830408 (6)
 DT Utility
 FS Granted
 LN.CNT 1669
 INCL INCLM: 530/387.000
 INCLS: 435/068.000; 435/172.300; 435/320.000; 435/252.300; 435/252.310;
 435/252.330; 435/252.340; 935/010.000; 935/015.000; 935/029.000;
 935/073.000; 530/388.000
 NCLM: 530/387.300
 NCLS: 435/069.600; 435/252.300; 435/252.310; 435/252.330; 435/252.340;
 435/320.100; 435/471.000; 530/388.850; 530/866.000; 530/867.000;
 930/010.000; 930/300.000
 IC [4]

ICM: C07K015-14
 ICS: C07K015-06; C12P021-00; C12N015-00; C12N001-20
 EXF 435/68; 435/172.3; 435/240; 435/253; 435/172.2; 435/317; 435/320;
 260/112B; 536/27; 935/11; 935/15; 935/27; 935/29; 935/73; 530/387;
 530/388
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his
 (FILE 'HOME' ENTERED AT 12:23:05 ON 26 SEP 2002)
 FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT
 12:23:48 ON 26 SEP 2002
 L1 41608 S ANTIBOD? AND LIBRAR?
 L2 137092 S POLYCLONA?
 L3 15758 S L2 AND L1
 L4 9841 S L3 AND PHAGE?
 L5 414 S L4 NOT PY=> 1994
 L6 339 DUP REM L5 (75 DUPLICATES REMOVED)
 L7 30 S L6 AND VARIABL? (A) REGION
 => s antibody (a) librar?
 L8 0 ANTIBOD (A) LIBRAR?
 => s antibody?(a)librar?
 L9 1668 ANTIBOD?(A) LIBRAR?
 => s 19 and polyclon?
 L10 628 L9 AND POLYCLON?
 => s l10 not py=
 MISSING TERM AFTER PY=
 Operators must be followed by a search term, L-number, or query name.
 => s l110 not py=>1994
 L110 NOT FOUND
 The L-number entered could not be found. To see the definition
 of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).
 => s l10 not py=> 1994
 '1994' NOT A VALID FIELD CODE
 5 FILES SEARCHED...
 L11 1 L10 NOT PY=> 1994
 => d l11
 L11 ANSWER 1 OF 1 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
 AN 1988:177831 BIOSIS
 DN BABS:89933
 TI MOLECULE CLONING AND AMINO ACID SEQUENCE OF HUMAN 5 LIPOXYGENASE.
 AU MATSUMOTO T; FUNK C D; RADMARK O; HOOG J-O; JORNVAL H; SAMUELSSON B
 CS CENTRAL RES. INST., JAPAN TOBACCO, INC., MIDORI-KU, YOKOHAMA, JPN.
 SO PROC NATL ACAD SCI U S A, (1988) 85 (1), 26-30.
 CODEN: PNAS86. ISSN: 0027-8424.
 FS BA; OLD
 LA English
 => d his
 (FILE 'HOME' ENTERED AT 12:23:05 ON 26 SEP 2002)
 FILE 'MEDLINE, CANCERLIT, BIOSIS, CONFSCI, EMBASE, USPATFULL' ENTERED AT

12:23:48 ON 26 SEP 2002

L1 41608 S ANTIBOD? AND LIBRAR?

L2 137092 S POLYCLONA?

L3 15758 S L2 AND L1

L4 9841 S L3 AND PHAGE?

L5 414 S L4 NOT PY-> 1994

L6 339 DUP REM L5 (75 DUPLICATES REMOVED)

L7 30 S L6 AND VARIABLE? (A) REGION

L8 0 S ANTIBOD? (A) LIBRAR?

L9 1668 S ANTIBOD? (A) LIBRAR?

L10 628 S L9 AND POLYCLON?

L11 1 S L10 NOT PY-> 1994

=> dup rem l10

PROCESSING COMPLETED FOR L10

L12 599 DUP REM L10 (29 DUPLICATES REMOVED)

=> s l12 and nucleic(a)acid(a) segment?

L13 48 L12 AND NUCLEIC(A) ACID(A) SEGMENT?

=> d 1-48

L13 ANSWER 1 OF 48 USPATFULL

AN 2002:251931 USPATFULL

TI Stress resistant retroviruses

IN Stemmer, Willem P.C., Los Gatos, CA, UNITED STATES

PI Otto, Edward, Falls Church, VA, UNITED STATES

AI 2002137889 AI 20020926

PRAI US 2001-954983 AI 20010917 (9)

US 2000-233398P 20000918 (60)

DT Utility

FS APPLICATION

LN.CNT 4898

INCL INCLM: 530/350.000

INCLS: 435/235.100; 435/069.100; 435/325.000; 536/023.720

NCL NCLM: 435/350.000

NCLS: 530/350.000

IC [7]

ICM: C12N007-01

ICS: C12P021-02; C07H021-04; C07K014-15; C12N005-06

L13 ANSWER 2 OF 48 USPATFULL

AN 2002:251101 USPATFULL

TI Novel nucleic acids and polypeptides

IN Tang, Y. Tom, San Jose, CA, UNITED STATES

Zhou, Ping, Cupertino, CA, UNITED STATES

Goodrich, Ryle, San Jose, CA, UNITED STATES

Liu, Chenghua, San Jose, CA, UNITED STATES

Asundi, Vinod, Foster City, CA, UNITED STATES

Wehrman, Tom, Stanford, CA, UNITED STATES

Yang, Yonghong, San Jose, CA, UNITED STATES

Dranac, Radoje T., Palo Alto, CA, UNITED STATES

US 2002137044 AI 20020926

AI 2001-774434 AI 20010130 (9)

RLI Continuation-in-part of Ser. No. US 2000-560875, filed on 27 Apr 2000, PENDING Continuation-in-part of Ser. No. US 2000-496914, filed on 3 Feb 2000, ABANDONED

DT Utility

FS APPLICATION

LN.CNT 5858

INCL INCLM: 435/006.000

INCLS: 536/023.100; 530/324.000; 530/387.900; 435/007.100; 435/069.100;

L13 ANSWER 3 OF 48 USPATFULL

AN 2002:246560 USPATFULL

TI Methods and compositions for inhibiting neoplastic cell growth

IN Edwards, Jean-Baptiste Dumas Milne, Paris, FRANCE

Duclert, Aymeric Saint-Maur, FRANCE

Bougueleret, Lydie, Petitlancy, SWITZERLAND

Clusel, Catherine, Montreuil-sous-Bois, FRANCE

Genset S.A., Paris, FRANCE (non-U.S. corporation)

PI US 6455280 B1 20020924

AI US 2000-750580 20001228 (9)

RLI Continuation-in-part of Ser. No. US 2000-599362, filed on 21 Jun 2000

Continuation-in-part of Ser. No. WO 2000-IB1011, filed on 21 Jun 2000

Continuation-in-part of Ser. No. US 1999-469099, filed on 21 Dec 1999

Continuation-in-part of Ser. No. WO 1999-IB2058, filed on 20 Dec 1999

PRAI US 1999-141032P 19990625 (60)

US 1998-113686P 19981222 (60)

DT Utility

FS GRANTED

LN.CNT 10937

INCL INCLM: 435/069.100

INCLS: 435/320.100; 530/350.000; 530/412.000; 530/417.000; 530/418.000;

NCL NCLM: 435/069.100

NCLS: 435/320.100; 530/350.000; 530/412.000; 530/417.000; 530/418.000;

IC [7]

ICM: C07K001-00

ICS: C07K014-00; C07K017-00; C12N015-00; C12N015-09; C12N015-63;

C12N015-70; C12N015-74; C12P021-06; A23J001-00; C07H021-04

EXF 530/350; 530/412; 530/417; 530/418; 435/320.1; 435/69.1; 536/23.1; 536/23.5

L13 ANSWER 4 OF 48 USPATFULL

AN 2002:243064 USPATFULL

TI EGF motif protein, EGFL6 materials and methods

IN Ford, John E., San Diego, CA, UNITED STATES

Yeung, George, Mountain View, CA, UNITED STATES

Zhou, Hua, Santa Clara, CA, UNITED STATES

US 2002132250 AI 20020919

AI 2001-981649 AI 20011015 (9)

RLI Continuation-in-part of Ser. No. US 2000-687860, filed on 13 Oct 2000, PENDING Continuation-in-part of Ser. No. US 1999-363316, filed on 28 Jul 1999, GRANTED, Pat. No. US 6392019

DT Utility

FS APPLICATION

LN.CNT 5958

INCL INCLM: 435/006.000

INCLS: 536/023.200

NCL NCLM: 435/006.000

NCLS: 536/023.200

IC [7]

ICM: C12Q001-68

ICS: C07H021-04

L13 ANSWER 5 OF 48 USPATFULL
 AN 2002:243051 USPATFULL
 TI Compositions and methods for the therapy and diagnosis of ovarian cancer
 IN Algate, Paul A., Issaquah, WA, UNITED STATES
 Jones, Robert, Seattle, WA, UNITED STATES
 Harlocker, Susan L., Seattle, WA, UNITED STATES
 PA Corixa Corporation, Seattle, WA, UNITED STATES, 98104 (U.S. corporation)
 PI US 2002:232237 AI 20020919
 AI US 2001-867701 AI 20010529 (9)
 PRAI US 2000-207484P 20000526 (60)
 DT Utility
 FS APPLICATION
 IN.CNT 25718
 INCL INCLM: 435/006.000
 INCL: 435/091.200
 NCL NCLM: 435/006.000
 NCL: 435/091.200
 IC [7]
 ICM: C12Q001-68
 ICS: C12P019-34
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 6 OF 48 USPATFULL
 AN 2002:235990 USPATFULL
 TI Novel nucleic acids and polypeptides
 IN Tang, Y. Tom, San Jose, CA, UNITED STATES
 Zhou, Ping, Cupertino, CA, UNITED STATES
 Goodrich, Ryle, San Jose, CA, UNITED STATES
 Liu, Chenghua, San Jose, CA, UNITED STATES
 Asundi, Vinod, Foster City, CA, UNITED STATES
 Ren, Feiyan, Cupertino, CA, UNITED STATES
 Zhao, Qing A., San Jose, CA, UNITED STATES
 Yang, Yonghong, San Jose, CA, UNITED STATES
 Wehrman, Tom, Stanford, CA, UNITED STATES
 Drmanac, Radoje T., Palo Alto, CA, UNITED STATES
 PI US 2002:28187 AI 20020912
 AI US 2000-728422 AI 20001130 (9)
 RLI Continuation-in-part of Ser. No. US 2000-560875, filed on 27 Apr 2000,
 PENDING Continuation-in-part of Ser. No. US 2000-496914, filed on 3 Feb
 2000, ABANDONED
 DT Utility
 FS APPLICATION
 IN.CNT 5355
 INCL INCLM: 514/012.000
 INCL: 530/350.000; 536/023.500; 435/069.100; 435/325.000; 435/320.100
 NCL NCLM: 514/012.000
 NCL: 530/350.000; 536/023.500; 435/069.100; 435/325.000; 435/320.100
 IC [7]
 ICM: A61K038-17
 ICS: C07K014-705; C12P021-02; C12N005-06
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 7 OF 48 USPATFULL
 AN 2002:235016 USPATFULL
 TI Novel nucleic acids and polypeptides
 IN Tang, Y. Tom, San Jose, CA, UNITED STATES
 Zhou, Ping, Cupertino, CA, UNITED STATES
 Goodrich, Ryle, San Jose, CA, UNITED STATES
 Asundi, Vinod, Foster City, CA, UNITED STATES
 Yang, Yonghong, San Jose, CA, UNITED STATES
 Zhang, Jie, Campbell, CA, UNITED STATES
 Wehrman, Tom, Stanford, CA, UNITED STATES
 Drmanac, Radoje T., Palo Alto, CA, UNITED STATES
 PI US 2002:27199 AI 20020912
 AI US 2001-815925 AI 20010322 (9)
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

RL1 Continuation-in-part of Ser. No. US 2000-560875, filed on 27 Apr 2000,
 PENDING Continuation-in-part of Ser. No. US 2000-496914, filed on 3 Feb
 2000, ABANDONED
 DT Utility
 FS APPLICATION
 IN.CNT 6503
 INCL INCLM: 424/085.100
 INCL: 435/006.000; 435/007.100; 435/069.500; 435/325.000; 435/320.100;
 530/351.000; 536/023.100
 NCL NCLM: 424/085.100
 NCL: 435/006.000; 435/007.100; 435/069.500; 435/325.000; 435/320.100;
 530/351.000; 536/023.100
 IC [7]
 ICM: C12Q001-68
 ICS: G01N033-53; C07H021-04; C12P021-02; C12N005-06; A61K038-19
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 8 OF 48 USPATFULL
 AN 2002:230849 USPATFULL
 TI Receptor-mediated gene delivery using bacteriophage vectors
 IN Larocca, David, Encinitas, CA, United States
 Baird, Andrew, San Diego, CA, United States
 Johnson, Wendy, Encinitas, CA, United States
 PA Selective Genetics, Inc., San Diego, CA, United States (U.S.
 corporation)
 PI US 6448083 BI 20020910
 AI US 1999-258584 19990226 (9)
 RLI Continuation-in-part of Ser. No. WO 1998-US17950, filed on 28 Aug 1998
 Continuation-in-part of Ser. No. US 1997-920396, filed on 29 Aug 1997,
 now patented, Pat. No. US 6054312
 DT Utility
 FS GRANTED
 IN.CNT 2896
 INCL INCLM: 435/456.000
 INCL: 435/320.100
 NCL NCLM: 435/456.000
 NCL: 435/320.100
 IC [7]
 ICM: C12N015-64
 ICS: C12N015-63
 EXF 435/456; 435/320.1

L13 ANSWER 9 OF 48 USPATFULL
 AN 2002:230601 USPATFULL
 TI Methods and materials relating to novel CD39-like polypeptides
 IN Ford, John, San Mateo, CA, United States
 Mulero, Julio J., Palo Alto, CA, United States
 PA Yeung, George, San Mateo, CA, United States
 PI US 6447771 BI 20020910
 AI US 1999-370265 19990809 (9)
 RLI Continuation-in-part of Ser. No. WO 1999-US16180, filed on 16 Jul 1999
 Continuation-in-part of Ser. No. US 1999-350836, filed on 9 Jul 1999,
 now patented, Pat. No. US 6387645 Continuation-in-part of Ser. No. US
 1999-273447, filed on 19 Mar 1999, now abandoned
 DT Utility
 FS GRANTED
 IN.CNT 4376
 INCL INCLM: 424/094.610
 NCL NCLM: 424/094.610
 IC [7]
 ICM: A61K038-47
 EXF 435/13; 435/18; 435/269; 435/267; 435/270; 424/94.61
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 10 OF 48 USPTFULL
 AN 2002:224704 USPTFULL
 TI CTLA4-C-gamma-4 fusion proteins
 IN Gray, Gary S., Brookline, MA, United States
 Carson, Jerry, Belmont, MA, United States
 Javanerian, Kahn, Lexington, MA, United States
 Renner, Paul D., Holliston, MA, United States
 Silver, Sandra, Boston, MA, United States
 PA Repligen Corporation, Needham, MA, United States (U.S. corporation)
 PI US 6444792 B1 20020903
 AI US 1999-227595 19990108 (9)
 RLI Division of Ser. No. US 1996-595590, filed on 2 Feb 1996
 DT Utility
 FS GRANTED
 LN.CNT 3031
 INCL INCLM: 530/387.300
 INCL INCLM: 530/387.100; 424/134.100
 NCL NCLM: 530/387.300
 NCL NCLM: 530/387.100; 424/134.100
 IC [7]
 ICM: A61K039-395
 EXF 530/387.1; 530/387.3; 530/388.8; 530/388.85; 424/134.1; 424/155.1;
 424/157.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L13 ANSWER 11 OF 48 USPTFULL
 AN 2002:221018 USPTFULL
 TI Antibody conjugate formulations for selectively inhibiting VEGF
 IN Thorpe, Philip E., Dallas, TX, UNITED STATES
 Brecken, Rolf A., Seattle, WA, UNITED STATES
 PA Board of Regents, The University of Texas System (U.S. corporation)
 PI US 2002119153 A1 20020829
 AI US 2001-998831 A1 20011130 (9)
 RLI Continuation of Ser. No. US 2000-561108, filed on 28 Apr 2000, PATENTED
 PRAI US 1999-131432P 19990428 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 10502
 INCL INCLM: 424/145.100
 INCL INCLM: 530/388.240; 424/133.100
 NCL NCLM: 424/145.100
 NCL NCLM: 530/388.240; 424/133.100
 IC [7]
 ICM: A61K039-395
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L13 ANSWER 12 OF 48 USPTFULL
 AN 2002:214215 USPTFULL
 TI Human beta-defensin-3 (HBD-3), a highly cationic beta-defensin
 IN antimicrobial peptide
 McCray, Paul B., Jr., Iowa City, IA, UNITED STATES
 Tack, Brian F., Iowa City, IA, UNITED STATES
 Jia, Hong Peng, Iowa City, IA, UNITED STATES
 Schutte, Brian C., Iowa City, IA, UNITED STATES
 PI US 2002115602 A1 20020822
 AI US 2001-872852 A1 20010601 (9)
 PRAI US 2000-208792P 20000601 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 3851
 INCL INCLM: 514/012.000
 INCL INCLM: 530/324.000

NCL NCLM: 514/012.000
 NCLM: 530/324.000
 IC [7]
 ICM: A61K038-17
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L13 ANSWER 13 OF 48 USPTFULL
 AN 2002:213441 USPTFULL
 TI CTLA4-Gamma4 fusion proteins
 IN Gray, Gary S., Brookline, MA, UNITED STATES
 Carson, Jerry, Belmont, MA, UNITED STATES
 Javanerian, Kahn, Lexington, MA, UNITED STATES
 Renner, Paul D., Holliston, MA, UNITED STATES
 Silver, Sandra, Boston, MA, UNITED STATES
 PI US 2002114814 A1 20020822
 AI US 2001-27075 A1 20011220 (10)
 RLI Continuation of Ser. No. US 1999-227595, filed on 8 Jan 1999, PENDING
 DT Division of Ser. No. US 1996-595590, filed on 2 Feb 1996, PENDING
 FS APPLICATION
 LN.CNT 3341
 INCL INCLM: 424/178.100
 INCL INCLM: 536/023.530; 435/069.100; 435/326.000; 435/320.100; 530/388.220
 NCL NCLM: 424/178.100
 NCL NCLM: 536/023.530; 435/069.100; 435/326.000; 435/320.100; 530/388.220
 IC [7]
 ICM: A61K039-395
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L13 ANSWER 14 OF 48 USPTFULL
 AN 2002:209359 USPTFULL
 TI Nucleic acids and polypeptides
 IN Tang, Y. Tom, San Jose, CA, United States
 Liu, Chenghua, San Jose, CA, United States
 Zhou, Ping, San Jose, CA, United States
 Asundi, Vinod, Foster City, CA, United States
 Zhang, Jie, Campbell, CA, United States
 Wang, Jian-Rui, Cupertino, CA, United States
 Xue, Aidong J., Sunnyvale, CA, United States
 Xu, Chongjun, San Jose, CA, United States
 Drmanac, Radoje T., Palo Alto, CA, United States
 Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
 PI US 6436703 B1 20020820
 AI US 2000-668680 20000922 (9)
 RLI Continuation-in-part of Ser. No. US 2000-649167, filed on 23 Aug 2000
 DT Continuation-in-part of Ser. No. US 2000-540217, filed on 31 Mar 2000
 FS Utility
 LN.CNT 5519
 INCL INCLM: 435/325.000
 INCL INCLM: 536/023.100; 536/023.500; 435/320.100
 NCL NCLM: 435/325.000
 NCL NCLM: 435/320.100; 536/023.100; 536/023.500
 IC [7]
 ICM: C12N015-12
 ICS: C12N005-00
 EXF 536/23.1; 536/23.5; 435/325; 435/320.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L13 ANSWER 15 OF 48 USPTFULL
 AN 2002:206605 USPTFULL
 TI Novel nucleic acids and polypeptides

IN Tang, Y. Tom, San Jose, CA, UNITED STATES
 Zhou, Ping, Cupertino, CA, UNITED STATES
 Goodrich, Ryle, San Jose, CA, UNITED STATES
 Liu, Chenghua, San Jose, CA, UNITED STATES
 Asundi, Vinod, Foster City, CA, UNITED STATES
 Wang, Jian-Rui, Cupertino, CA, UNITED STATES
 Wang, Durrui, Poway, CA, UNITED STATES
 Yamazaki, Victoria, Redwood Shores, CA, UNITED STATES
 Ujwal, Manusha L., Gaithersburg, MD, UNITED STATES
 Drmanac, Radoje T., Palo Alto, CA, UNITED STATES
 US 2002111302 AI 20020815
 US 2000-728952 AI 20001130 (9)
 Utility
 FS APPLICATION
 LN.CNT 4863
 INCL INCLM: 514/012.000
 INCLS: 530/350.000; 536/023.100; 435/069.100; 435/325.000; 435/320.100
 NCL NCLM: 514/012.000
 NCLS: 530/350.000; 536/023.100; 435/069.100; 435/325.000; 435/320.100
 IC [7]
 ICM: A61K038-17
 ICS: C07H021-04; C07K014-435; C12P021-02; C12N005-06
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 16 OF 48 USPTATFULL
 AN 2002:199275 USPTATFULL
 TI Methods and compositions relating to bone-derived growth factor-like polypeptides
 IN Ford, John E., San Mateo, CA, UNITED STATES
 PI US 2002107386 AI 20020808
 US 2002-62394 AI 20020201 (10)
 RLI Continuation of Ser. No. US 1998-157305, filed on 18 Sep 1998, PENDING
 DT Utility
 FS APPLICATION
 LN.CNT 3046
 INCL INCLM: 536/023.500
 INCLS: 435/006.000; 435/069.400; 435/325.000; 435/320.100; 530/399.000
 NCL NCLM: 536/023.500
 NCLS: 435/006.000; 435/069.400; 435/325.000; 435/320.100; 530/399.000
 IC [7]
 ICM: C120001-68
 ICS: C07H021-04; C12P021-02; C12N005-06; C07K014-51
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 17 OF 48 USPTATFULL
 AN 2002:191548 USPTATFULL
 TI Novel Fab fragment libraries and methods for their use
 IN Hooogenboom, Hendricus Renerus Jacobus Mattheus, Maastricht, NETHERLANDS
 PI US 2002102613 AI 20020801
 AI US 2001-988899 AI 20011119 (9)
 RLI Continuation of Ser. No. WO 2000-US13682, filed on 18 May 2000, UNKNOWN
 PRAI EP 1999-201558 19990518
 DT Utility
 FS APPLICATION
 LN.CNT 4310
 INCL INCLM: 435/007.100
 INCLS: 435/320.100; 530/388.100; 435/069.100; 435/326.000; 536/023.530
 NCL NCLM: 435/007.100
 NCLS: 435/320.100; 530/388.100; 435/069.100; 435/326.000; 536/023.530
 IC [7]
 ICM: G01N033-53
 ICS: C07H021-04; C12P021-02; C12N005-06; C07K016-00
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 18 OF 48 USPTATFULL
 AN 2002:191539 USPTATFULL
 TI Full-length human cDNAs encoding potentially secreted proteins
 IN Milne Edwards, Jean-Baptiste Dumas, Paris, FRANCE
 Bouguetel, Lydie, Petit Lancy, SWITZERLAND
 Jobert, Severin, Paris, FRANCE
 PI US 2002102604 AI 20020801
 US 2000-731872 AI 20001207 (9)
 PRAI US 1999-169629P 19991208 (60)
 US 2000-187470P 20000306 (60)
 DT Utility
 FS APPLICATION
 LN.CNT 28061
 INCL INCLM: 435/007.100
 INCLS: 536/023.100; 530/350.000
 NCL NCLM: 435/007.100
 NCLS: 536/023.100; 530/350.000
 IC [7]
 ICM: G01N033-53
 ICS: C07H021-02; C07H021-04; C07K001-00; C07K014-00; C07K017-00
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 19 OF 48 USPTATFULL
 AN 2002:188224 USPTATFULL
 TI Assays involving an IL-1 receptor antagonist
 IN Ford, John, San Mateo, CA, United States
 Pace, Ann, Scotts Valley, CA, United States
 PA Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
 PI US 6426191 BI 20020730
 US 1999-457626 19991208 (9)
 RLI Continuation-in-part of Ser. No. US 1999-417455, filed on 13 Oct 1999, now patented, Pat. No. US 6294655 Continuation-in-part of Ser. No. US 1999-348942, filed on 7 Jul 1999, now patented, Pat. No. US 6337072 Continuation-in-part of Ser. No. US 1999-287210, filed on 5 Apr 1999, now abandoned Continuation-in-part of Ser. No. US 1999-251370, filed on 17 Feb 1999, now abandoned Continuation-in-part of Ser. No. US 1998-127698, filed on 31 Jul 1998, now abandoned Continuation-in-part of Ser. No. US 1999-229591, filed on 13 Jan 1999, now abandoned Continuation of Ser. No. US 1998-99818, filed on 19 Jun 1998, now abandoned Continuation of Ser. No. US 127698 Continuation of Ser. No. US 99818 Continuation-in-part of Ser. No. US 1998-82364, filed on 20 May 1998, now abandoned Continuation-in-part of Ser. No. US 1998-79909, filed on 15 May 1998, now abandoned Continuation-in-part of Ser. No. US 1998-55010, filed on 3 Apr 1998, now abandoned
 DT Utility
 FS GRANTED
 LN.CNT 5305
 INCL INCLM: 435/007.800
 INCLS: 435/007.100; 435/007.200; 436/501.000; 436/502.000
 NCL NCLM: 435/007.800
 NCLS: 435/007.100; 435/007.200; 436/501.000; 436/512.000
 IC [7]
 ICM: G01N033-53
 EXF 536/23.5: 530/351; 435/69.1; 435/6; 435/7.1; 435/7.2; 435/7.8; 436/501; 436/512
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 20 OF 48 USPTATFULL
 AN 2002:174946 USPTATFULL
 TI Chimeric polyclonal antibodies
 IN Buechler, Joe, Carlsbad, CA, United States
 Valkirs, Gunars, Escondido, CA, United States
 Gray, Jeff, Solana Beach, CA, United States
 PA Biosite Diagnostics, Inc., San Diego, CA, United States (U.S.)

corporation)
 PI US 6420113 B1 20020716
 AI US 1999-410903 19991002 (9)
 RLI Continuation-in-part of Ser. No. WO 1998-US6704, filed on 3 Apr 1998
 Continuation-in-part of Ser. No. US 1997-835159, filed on 4 Apr 1997
 Continuation-in-part of Ser. No. US 1997-832985, filed on 4 Apr 1997,
 now patented, Pat. No. US 6057098
 DT Utility
 FS GRANTED
 LN.CNT 3885
 INCL INCLM: 435/006.000
 INCLM: 435/007.100; 435/069.100; 435/320.100; 435/DIG.001; 435/DIG.002;
 435/DIG.003; 435/DIG.014; 435/DIG.017; 536/023.100;
 536/023.530
 NCL NCLM: 435/006.000
 NCLM: 435/007.100; 435/069.100; 435/320.100; 435/DIG.001; 435/DIG.002;
 435/DIG.003; 435/DIG.014; 435/DIG.017; 536/023.100;
 536/023.530
 IC [7]
 ICM: C12P001-68
 ICS: C12P021-06; C07H021-02
 EXF 435/6; 435/7.1; 435/7.8; 435/91.4; 435/471; 435/489; 435/69.1; 435/69.6;
 435/320.1; 435/DIG.1; 435/DIG.2; 435/DIG.3; 435/DIG.4; 435/DIG.14;
 435/DIG.17; 536/23.1; 536/23.53
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L13 ANSWER 21 OF 48 USPATFULL
 AN 2002:167884 USPATFULL
 TI Antibody conjugate kits for selectively inhibiting VEGF
 IN Thorpe, Philip E., Dallas, TX, United States
 Brekken, Rolf A., Seattle, WA, United States
 PA Board of Regents, The University of Texas System, Austin, TX, United
 States (U.S. corporation)
 PI US 6416758 B1 20020709
 AI US 2000-561526 20000428 (9)
 PRAI US 1999-131432P 19990428 (60)
 DT Utility
 FS GRANTED
 LN.CNT 10439
 INCL INCLM: 424/145.100
 INCLM: 424/001.490; 424/001.530; 424/001.690; 424/009.200; 424/009.300;
 424/133.100; 424/134.100; 424/135.100; 424/141.100; 424/142.100;
 424/145.100; 424/178.100; 424/181.100; 424/183.100; 424/189.100;
 424/195.110; 435/007.230; 435/069.600; 435/069.700;
 435/070.210; 435/810.000; 530/387.300; 530/388.100; 530/388.150;
 530/388.240; 530/391.300; 530/391.700; 530/391.900
 NCL NCLM: 424/145.100
 NCLM: 424/001.490; 424/001.530; 424/001.690; 424/009.200; 424/009.300;
 424/133.100; 424/134.100; 424/135.100; 424/141.100; 424/142.100;
 424/178.100; 424/179.100; 424/181.100; 424/183.100; 424/189.110;
 435/007.230; 435/069.600; 435/069.700; 435/070.210;
 435/810.000; 530/387.300; 530/388.100; 530/388.150; 530/388.240;
 530/391.300; 530/391.700; 530/391.900
 IC [7]
 ICM: A61K038-36
 ICS: C12P021-08; C07K016-22
 EXF 424/9.2; 424/9.3; 424/133.1; 424/134.1; 424/135.1; 424/141.1; 424/142.1;
 424/145.1; 424/178.1; 424/181.1; 424/183.1; 424/195.11; 424/179.1;
 424/1.49; 424/1.53; 424/1.69; 530/387.3; 530/388.15; 530/388.24;
 530/391.3; 530/391.5; 530/391.7; 530/391.9; 435/69.6; 435/69.7;
 435/69.1; 435/70.21; 435/7.23; 435/810
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L13 ANSWER 22 OF 48 USPATFULL

2002:157026 USPATFULL
 AN MEMBER OF THE IMMUNOGLOBULIN SUPERFAMILY AND USES THEREOF
 TI FORD, JOHN, SAN MATEO, CA, UNITED STATES
 IN YOUNG, GEORGE, SAN MATEO, CA, UNITED STATES
 PI US 2002081625 AI 20020627
 AI US 1999-417791 AI 19991014 (9)
 DT Utility
 FS APPLICATION
 LN.CNT 4010
 INCL INCLM: 435/007.100
 INCLM: 536/023.530
 NCL NCLM: 435/007.100
 NCLM: 536/023.530
 IC [7]
 ICM: G01N033-53
 ICS: C07H021-04; C12P013-14; C12N005-02
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L13 ANSWER 23 OF 48 USPATFULL
 AN 2002:152392 USPATFULL
 TI Methods of screening open reading frames to determine whether they
 encode polypeptides with an ability to generate an immune response
 IN Sykes, Kathryn F., Dallas, TX, United States
 Johnston, Stephen Albert, Dallas, TX, United States
 PA Board of Regents, The University of Texas System, Austin, TX, United
 States (U.S. corporation)
 PI US 6410241 B1 20020625
 AI US 2000-535366 20000324 (9)
 PRAI US 1999-125864P 19990324 (60)
 US 1999-127222P 19990331 (60)
 DT Utility
 FS GRANTED
 LN.CNT 4001
 INCL INCLM: 435/006.000
 INCLM: 435/007.210
 NCL NCLM: 435/006.000
 NCLM: 435/007.210
 IC [7]
 ICM: C12Q001-68
 EXF 435/6; 435/7.1; 435/325; 435/7.21; 514/44
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.
 L13 ANSWER 24 OF 48 USPATFULL
 AN 2002:143940 USPATFULL
 TI Cancer treatment methods using antibodies to aminophospholipids
 IN Thorpe, Philip E., Dallas, TX, United States
 Ran, Sophia, Dallas, TX, United States
 PA Board of Regents, The University of Texas System, Austin, TX, United
 States (U.S. corporation)
 PI US 6406693 B1 20020618
 AI US 1999-351543 19990712 (9)
 PRAI US 1998-110608P 19981202 (60)
 US 1998-92672P 19980713 (60)
 DT Utility
 FS GRANTED
 LN.CNT 7541
 INCL INCLM: 424/130.100
 INCLM: 424/132.100; 424/133.100; 424/135.100; 424/138.100; 424/141.100;
 424/152.100; 424/184.100; 530/387.100; 435/006.000
 NCL NCLM: 424/130.100
 NCLM: 424/132.100; 424/133.100; 424/135.100; 424/138.100; 424/141.100;
 424/152.100; 424/184.100; 435/006.000; 530/387.100
 IC [7]
 ICM: A61K039-395

ICS: C07K016-00; C07K016-28; C07K016-30; C12Q001-68
 EXF 424/130.1; 424/184.1; 424/132.1; 424/133.1; 424/135.1; 424/138.1;
 424/141.1; 424/152.1; 530/387.1; 435/6
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 25 OF 48 USPTAFULL
 AN 2002:119584 USPTAFULL
 TI Novel nucleic acids and polypeptides
 IN Tang, Y. Tom, San Jose, CA, UNITED STATES
 Liu, Chenghua, San Jose, CA, UNITED STATES
 Zhou, Ping, Cupertino, CA, UNITED STATES
 Asundi, Vinod, Foster City, CA, UNITED STATES
 Ren, Feiyan, Cupertino, CA, UNITED STATES
 Zhang, Jie, Campbell, CA, UNITED STATES
 Zhao, Qing A., San Jose, CA, UNITED STATES
 Xue, Aidong J., Sunnyvale, CA, UNITED STATES
 Goodrich, Ryle, San Jose, CA, UNITED STATES
 Wehrman, Tom, Stanford, CA, UNITED STATES
 Dtranac, Radoje T., Palo Alto, CA, UNITED STATES
 PI US 2002061567 AI 20020523
 AI US 2000-728711 AI 20001130 (9)
 RLI Continuation-in-part of Ser. No. US 2000-649167, filed on 23 Aug 2000,
 PENDING Continuation-in-part of Ser. No. US 2000-540217, filed on 31 Mar
 2000, PENDING
 DT Utility
 FS APPLICATION
 LN.CNT 5921
 INCL INCLM: 435/183.000
 INCLS: 435/069.100; 435/325.000; 435/320.100; 536/023.200
 NCL NCLM: 435/183.000
 NCLS: 435/069.100; 435/325.000; 435/320.100; 536/023.200
 IC [7]
 ICM: C12N009-00
 ICS: C07H021-04; C12P021-02; C12N005-06
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 26 OF 48 USPTAFULL
 AN 2002:116388 USPTAFULL
 TI Antibodies specific for EGF motif proteins
 IN Ford, John, 2763 S. Norfolk, #210, San Mateo, CA, United States 94403
 Yeung, George, 102 Magnolia La., Mountainview, CA, United States 94043
 PI US 6392019 BI 20020521
 AI US 1999-363316 19990728 (9)
 RLI Continuation-in-part of Ser. No. US 1999-249697, filed on 12 Feb 1999
 Continuation-in-part of Ser. No. US 1997-968800, filed on 22 Nov 1997,
 now abandoned
 DT Utility
 FS GRANTED
 LN.CNT 3505
 INCL INCLM: 530/387.900
 INCLS: 530/300.000; 530/350.000; 530/387.100; 530/388.100; 530/389.100
 NCL NCLM: 530/387.900
 NCLS: 530/300.000; 530/350.000; 530/387.100; 530/388.100; 530/389.100
 IC [7]
 ICM: C07K002-00
 ICS: C07K014-00; C07K016-00; C07K016-18
 EXF 435/331.3; 530/387.1; 530/387.9; 530/388.1; 530/388.15; 530/389.1;
 530/391.3; 530/300; 530/350; 530/388.23; 530/388.24; 530/389.2
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 27 OF 48 USPTAFULL
 AN 2002:116387 USPTAFULL
 TI EGF MOTIF protein obtained from a cDNA library of fetal liver-spleen
 IN Ford, John, San Mateo, CA, United States

Yeung, George, Mountainview, CA, United States
 Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
 PI US 6392018 BI 20020521
 AI US 1999-249697 19990212 (9)
 RLI Continuation-in-part of Ser. No. US 1997-968800, filed on 22 Nov 1997,
 now abandoned
 DT Utility
 FS GRANTED
 LN.CNT 3353
 INCL INCLM: 530/351.000
 INCLS: 530/350.000; 530/324.000; 530/326.000; 514/002.000; 424/085.100
 NCL NCLM: 530/351.000
 NCLS: 424/085.100; 530/324.000; 530/326.000; 530/350.000
 IC [7]
 ICM: C07K017-00
 ICS: C07K007-04; A61K045-00; A61K038-00
 EXF 530/350; 530/300; 530/324; 530/351; 530/326; 530/327; 435/69.1;
 435/320.1; 435/325; 435/252.3; 435/7.1; 424/130.1; 420/130.1; 536/23.5
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 28 OF 48 USPTAFULL
 AN 2002:112286 USPTAFULL
 TI Novel interleukin-3 and uses thereof
 IN Ford, John, San Mateo, CA, UNITED STATES
 PA Hyseq, Inc. (U.S. corporation)
 PI US 2002058018 AI 20020516
 AI US 2001-792246 AI 20010223 (9)
 RLI Continuation of Ser. No. US 1999-376732, filed on 17 Aug 1999, UNKNOWN
 DT Utility
 FS APPLICATION
 LN.CNT 5626
 INCL INCLM: 424/085.200
 INCLS: 435/069.520; 435/325.000; 435/007.100; 536/023.500; 530/351.000
 NCL NCLM: 424/085.200
 NCLS: 435/069.520; 435/325.000; 435/007.100; 536/023.500; 530/351.000
 IC [7]
 ICM: A61K038-20
 ICS: C01N033-53; C07H021-04; C12N005-06; C07K014-54
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 29 OF 48 USPTAFULL
 AN 2002:108835 USPTAFULL
 TI Methods and materials relating to novel CD39-like polypeptides
 IN Ford, John, San Mateo, CA, United States
 Mulero, Julio J., Palo Alto, CA, United States
 PA Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
 PI US 6387645 BI 20020514
 AI US 1999-350836 19990709 (9)
 RLI Continuation-in-part of Ser. No. US 1999-273447, filed on 19 Mar 1999,
 now abandoned Continuation-in-part of Ser. No. US 1998-122449, filed on
 24 Jul 1998, now abandoned Continuation-in-part of Ser. No. US
 1998-118205, filed on 16 Jul 1998, now abandoned
 DT Utility
 FS GRANTED
 LN.CNT 2423
 INCL INCLM: 435/021.000
 INCLS: 435/018.000
 NCL NCLM: 435/021.000
 NCLS: 435/018.000
 IC [7]
 ICM: C12Q001-42
 EXF 435/7.1; 435/18; 435/21
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 30 OF 48 USPATFULL
AN 2002:81614 USPATFULL
TI Interleukin-1 Hy2 materials and methods
IN Ballinger, Dennis G., Menlo Park, CA, United States
Pace, Ann M., Scotts Valley, CA, United States
Lin, Hai Shan, Castro Valley, CA, United States
PA Hysq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI US 6372892 B1 20020416
AI US 2000-522964
RLI Continuation-in-part of Ser. No. US 1999-316086, filed on 20 May 1999,
now patented, Pat. No. US 6175532

DT Utility
FS GRANTED
LN.CNT 4690
INCL INCLM: 530/389.200
INCLS: 350/351.000
NCLM: 530/389.200
NCL NCLM: 530/350.000; 530/351.000
IC [7]
ICM: C07K017-00
ICS: C07K016-00
EXF 530/351; 530/389.2
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 31 OF 48 USPATFULL
AN 2002:78408 USPATFULL
TI Prostate cancer-related compositions, methods, and kits based on DNA
macroarray proteomics platforms
IN Stearns, Mark, Villanova, PA, United States
Hu, Youji, Gulph Mills, PA, United States
Wang, Min, Gulph Mills, PA, United States
PI US 2002042062 A1 20020411
AI US 2001-813380 A1 20010321 (9)
RLI Continuation-in-part of Ser. No. US 2000-522981, filed on 24 Sep 2000,
UNKNOWN

PRAI US 1999-155865P 19990924 (60)
DT Utility
FS APPLICATION
LN.CNT 6916
INCL INCLM: 435/006.000
INCLS: 435/007.230; 435/325.000; 435/069.300; 536/023.500; 530/350.000;
435/183.000
NCLM: 435/006.000
NCL NCLM: 435/007.230; 435/325.000; 435/069.300; 536/023.500; 530/350.000;
435/183.000
IC [7]
ICM: C12M001-68
ICS: G01N033-574; C07H021-04; C12N009-00; C12P021-02; C12N005-06;
C07K014-47
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 32 OF 48 USPATFULL
AN 2002:70108 USPATFULL
TI Polynucleotides encoding IL-1 Hy2 polypeptides
IN Ballinger, Dennis G., Menlo, CA, United States
Ford, John, San Mateo, CA, United States
Ho, Alice Suk-Yue, Union City, CA, United States
Lin, Hai Shan, Castro Valley, CA, United States
Pace, Ann M., Scotts Valley, CA, United States
PA Hysq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI US 6365726 B1 20020402
AI US 2000-578458
RLI Continuation-in-part of Ser. No. US 2000-522964, filed on 10 Mar 2000,
Continuation-in-part of Ser. No. US 1999-316081, filed on 20 May 1999,

now patented, Pat. No. US 6339141

DT Utility
FS GRANTED
LN.CNT 4803
INCL INCLM: 536/023.520
INCLS: 536/023.100; 536/023.500; 536/024.310; 435/069.100; 435/069.520;
435/320.100
NCLM: 536/023.520
NCL NCLM: 435/069.100; 435/069.520; 435/320.100; 536/023.100; 536/023.500;
536/024.310
IC [7]
ICM: C07H021-04
ICS: C12P021-06; C12N015-00; C12N015-06
EXF 435/69.1; 435/69.52; 435/320.1; 435/23.1; 536/23.5; 536/23.52;
536/24.31; 530/350; 530/357
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 33 OF 48 USPATFULL
AN 2002:67174 USPATFULL
TI Novel matrix metalloproteinase (MMP-25) expressed in skin cells
IN Wang, Kai, Bellevue, WA, United States
Smith, Ryan, Seattle, WA, United States
Fajardo, Mark, Shoreline, WA, United States
Moss, Patrick, Shoreline, WA, United States
Schatzman, Randall C., Shoreline, WA, United States LR
PI US 2002037827 A1 20020328
AI US 2001-801196 A1 20010306 (9)
PRAI US 2000-187196P 20000306 (60)
DT Utility
FS APPLICATION
LN.CNT 4015
INCL INCLM: 514/001.000
INCLS: 435/226.000; 800/008.000; 435/325.000; 435/069.100; 536/023.200
NCLM: 514/001.000
NCL NCLM: 435/226.000; 800/008.000; 435/325.000; 435/069.100; 536/023.200
IC [7]
ICM: A61K031-00
ICS: A01K067-00; C07H021-04; C12N009-64; C12N005-06; C12P021-02
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 34 OF 48 USPATFULL
AN 2002:39654 USPATFULL
TI Methods and compositions relating to CD39-like polypeptides and nucleic
acids
IN Chadwick, Brian Paul, Allston, MA, United States
Frischauf, Anna-Maria, London, UNITED KINGDOM
PA HYSQ, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI US 6350447 B1 20020226
AI US 1999-240639 19990129 (9)
DT Utility
FS GRANTED
LN.CNT 4954
INCL INCLM: 424/094.600
INCLS: 435/195.000; 514/012.000; 530/350.000
NCLM: 424/094.600
NCL NCLM: 435/195.000; 514/012.000; 530/350.000
IC [7]
ICM: A61K038-46
ICS: C12N009-14; C07K014-435
EXF 435/195; 514/12; 424/94.6; 530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 35 OF 48 USPATFULL
AN 2002:19060 USPATFULL

TI Antibody conjugate compositions for selectively inhibiting VEGF
IN Thorpe, Philip E., Dallas, TX, United States
PA Brekken, Rolf A., Seattle, WA, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 6342221 BI 20020129
AI US 2000-561108 19990428 (9)
PRAI US 1999-131432P 19990428 (60)
DT Utility
FS GRANTED
LN.CNT 10492
LNCL INCLM: 424/178.100
INCLS: 424/130.100; 424/179.100; 424/181.100; 424/183.100; 424/193.100;
424/195.110; 424/001.490; 424/001.530; 424/009.340; 424/009.340;
424/009.600; 435/007.210; 435/069.100; 435/070.210; 435/810.000;
435/007.230; 435/007.100; 530/391.100; 530/391.300; 530/391.500;
530/391.700; 530/391.900
NCL NCLM: 424/178.100
NCLS: 424/001.490; 424/001.530; 424/009.340; 424/009.340; 424/009.600;
424/130.100; 424/179.100; 424/181.100; 424/183.100; 424/193.100;
424/195.110; 435/007.100; 435/007.210; 435/007.230; 435/069.100;
435/070.210; 435/810.000; 530/391.100; 530/391.300; 530/391.500;
530/391.700; 530/391.900
IC [7]
ICM: A61K039-44
ICS: A61K039-395
EXF 424/130.1; 424/133.1; 424/134.1; 424/135.1; 424/141.1; 424/142.1;
424/143.1; 424/178.1; 424/181.1; 424/183.1; 424/195.11; 424/179.1;
424/1.49; 424/1.53; 424/1.69; 424/193.1; 424/9.3; 424/9.34; 424/9.6;
530/387.1; 530/387.3; 530/388.1; 530/388.15; 530/388.22; 530/391.1;
530/391.3; 530/391.5; 530/391.7; 530/391.9; 530/809; 530/864; 530/865;
530/866; 435/7.1; 435/69.1; 435/70.21; 435/810; 435/7.21; 435/7.23
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 36 OF 48 USPATFULL
AN 2002.19058 USPATFULL
TI Antibody compositions for selectively inhibiting VEGF
IN Thorpe, Philip E., Dallas, TX, United States
PA Brekken, Rolf A., Seattle, WA, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 6342219 BI 20020129
AI US 2000-561500 20000428 (9)
PRAI US 1999-131432P 19990428 (60)
DT Utility
FS GRANTED
LN.CNT 10403
LNCL INCLM: 424/145.100
INCLS: 424/133.100; 424/134.100; 424/135.100; 424/141.100; 424/142.100;
424/143.100; 435/069.100; 435/335.000; 435/810.000; 530/387.100;
530/387.300; 530/388.100; 530/388.150; 530/388.230; 530/391.100;
530/391.300; 530/391.500; 530/391.700; 530/809.000; 530/864.000;
530/865.000; 530/866.000
NCL NCLM: 424/145.100
NCLS: 424/133.100; 424/134.100; 424/135.100; 424/141.100; 424/142.100;
424/143.100; 435/069.100; 435/335.000; 435/810.000; 530/387.100;
530/387.300; 530/388.100; 530/388.150; 530/388.230; 530/391.100;
530/391.300; 530/391.500; 530/391.700; 530/809.000; 530/864.000;
530/865.000; 530/866.000
IC [7]
ICM: A61K039-395
ICS: C12P021-08; C07K016-00
EXF 424/130.1; 424/133.1; 424/134.1; 424/135.1; 424/141.1; 424/142.1;
424/143.1; 424/145.1; 435/810; 435/69.1; 435/335; 530/387.1; 530/387.3;

530/388.1; 530/388.15; 530/388.23; 530/391.1; 530/391.3; 530/391.5;
530/391.7; 530/809; 530/864; 530/865; 530/866
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 37 OF 48 USPATFULL
AN 2002.16906 USPATFULL
TI Novel nucleic acids and polypeptides
IN Tang, Y. Tom, San Jose, CA, UNITED STATES
Zhou, Ping, Cupertino, CA, UNITED STATES
Goodrich, Ryle, San Jose, CA, UNITED STATES
Liu, Chenghua, San Jose, CA, UNITED STATES
Asundi, Vinod, Foster City, CA, UNITED STATES
Xue, Aidong J., Sunnyvale, CA, UNITED STATES
Zhang, Jie, Campbell, CA, UNITED STATES
Zhao, Qing A., San Jose, CA, UNITED STATES
Ren, Feiyang, Cupertino, CA, UNITED STATES
Dmanac, Radoje T., Palo Alto, CA, UNITED STATES
PI US 2002009786 AI 20020124
AI US 2000-728628 AI 20001201 (9)
RLI Continuation-in-part of Ser. No. US 2000-552929, filed on 18 Apr 2000,
UNKNOWN
DT Utility
FS APPLICATION
LN.CNT 5748
LNCL INCLM: 435/183.000
INCLS: 435/059.100; 435/325.000; 536/023.200
NCL NCLM: 435/183.000
NCLS: 435/059.100; 435/325.000; 536/023.200
IC [7]
ICM: C12P021-02
ICS: C07H021-04; C12N009-00; C12N005-06
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 38 OF 48 USPATFULL
AN 2002.9923 USPATFULL
TI Interleukin-1 Hy2 materials and methods
IN Ballinger, Dennis G., Menlo Park, CA, United States
Pace, Ann M., Scotts Valley, CA, United States
PA Hycey Inc., Sunnydale, CA, United States (U.S. corporation)
PI US 6339141 BI 20020115
AI US 1999-316081 19990520 (9)
DT Utility
FS GRANTED
LN.CNT 4019
LNCL INCLM: 530/351.000
INCLS: 424/085.200; 424/143.100; 424/145.100
NCL NCLM: 530/351.000
NCLS: 424/085.200; 424/143.100; 424/145.100
IC [7]
ICM: C07K017-00
ICS: A61K045-00; A61K039-395
EXF 530/357; 424/85.2; 424/143.1; 424/145.1
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 39 OF 48 USPATFULL
AN 2002.5759 USPATFULL
TI Interleukin-1 receptor antagonist and recombinant production thereof
IN Ford, John, San Mateo, CA, United States
Pace, Ann, Scotts Valley, CA, United States
PA Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI US 6337072 BI 20020108
AI US 1999-348942 19990707 (9)
RLI Continuation-in-part of Ser. No. US 1999-287210, filed on 5 Apr 1999,
now abandoned Continuation-in-part of Ser. No. US 1999-251370, filed on

17 Feb 1999, now abandoned Continuation-in-part of Ser. No. US 1999-229591, filed on 13 Jan 1999, now abandoned Continuation-in-part of Ser. No. US 1998-127698, filed on 31 Jul 1998, now abandoned Continuation of Ser. No. US 1998-99818, filed on 19 Jun 1998, now abandoned Continuation of Ser. No. US 1998-82364, filed on 20 May 1998, now abandoned Continuation-in-part of Ser. No. US 1998-79909, filed on 15 May 1998, now abandoned Continuation-in-part of Ser. No. US 1998-55010, filed on 3 Apr 1998, now abandoned

PRAI WO 1999-US4291 19990405
 DT Utility
 FS GRANTED
 LN.CNT 5025
 INCL INCLM: 424/198.100
 INCL INCLM: 536/023.500; 435/069.100; 435/069.520; 435/325.000; 435/252.300; 435/320.100; 514/002.000; 530/350.000; 530/402.000; 424/001.690
 NCL NCLM: 424/198.100
 NCL NCLM: 424/001.690
 NCL NCLM: 424/001.690; 435/069.100; 435/069.520; 435/252.300; 435/320.100; 435/325.000; 514/002.000; 530/350.000; 530/402.000; 536/023.500
 IC [7]
 ICM: C07K014-54
 ICS: C07K021-04; A61K038-20
 EXF 530/350; 530/351; 435/69.1; 435/69.5; 435/69.52; 435/325; 435/252.3; 435/320.1; 536/23.5; 514/2; 424/198.1; 424/1.69
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 40 OF 48 USPATFULL
 AN 2002:926 USPATFULL
 TI Methods and materials relating to CD39-like polypeptides
 IN Ford, John, San Mateo, CA, United States
 Mulero, Julio J., Palo Alto, CA, United States
 Yeung, George, Mountain View, CA, United States
 PA Ryseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
 PI US 6335013 B1 20020101
 AI US 2000-608285 20000630 (9)
 RLI Continuation-in-part of Ser. No. US 2000-583231, filed on 26 May 2000
 Continuation-in-part of Ser. No. US 2000-557800, filed on 25 Apr 2000
 Continuation-in-part of Ser. No. US 2000-481238, filed on 11 Jan 2000
 Continuation-in-part of Ser. No. US 1999-370265, filed on 9 Aug 1999
 Continuation-in-part of Ser. No. WO 1999-US16180, filed on 16 Jul 1999
 Continuation-in-part of Ser. No. US 1999-350836, filed on 9 Jul 1999
 Continuation-in-part of Ser. No. US 1999-273447, filed on 19 Mar 1999
 DT Utility
 FS GRANTED
 LN.CNT 4738
 INCL INCLM: 424/094.610
 INCL INCLM: 514/012.000
 NCL NCLM: 424/094.610
 NCL NCLM: 514/012.000
 IC [7]
 ICM: A61K038-47
 EXF 435/13; 435/18; 424/94.61; 514/12
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 41 OF 48 USPATFULL
 AN 2001:196503 USPATFULL
 TI Cancer treatment methods using therapeutic conjugates that bind to aminophospholipids
 IN Thorpe, Philip E., Dallas, TX, United States
 PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
 PI US 6312694 B1 20011106

AI US 1999-351457 19990712 (9)
 PRAI US 1998-92589P 19980713 (60)
 DT Utility 19981202 (60)
 FS GRANTED
 LN.CNT 8243
 INCL INCLM: 424/178.100
 INCL INCLM: 424/133.100; 424/134.100; 424/135.100; 424/136.100; 424/137.100; 424/141.100; 424/142.100; 424/143.100; 424/181.100; 424/193.100; 514/012.000; 530/387.100; 530/388.100
 NCL NCLM: 424/178.100
 NCL NCLM: 424/133.100; 424/134.100; 424/135.100; 424/136.100; 424/137.100; 424/141.100; 424/142.100; 424/143.100; 424/181.100; 424/193.100; 514/012.000; 530/387.100; 530/388.100
 IC [7]
 ICM: A61K039-395
 ICS: C12P021-08; C07K016-00
 EXF 514/12; 424/133.1; 424/135.1; 424/136.1; 424/137.1; 424/141.1; 424/142.1; 424/143.1; 424/178.1; 424/181.1; 424/193.1; 530/387.1; 530/388.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 42 OF 48 USPATFULL
 AN 2001:178817 USPATFULL
 TI Method for generating libraries of antibody genes comprising amplification of diverse antibody DNAs and methods for using these libraries for the production of diverse antigen combining molecules
 IN Wiegler, Michael H., Lloyd Harbor, NY, United States
 PA Sratagene, San Diego, CA, United States (U.S. corporation)
 PI US 6303313 B1 20011016
 AI US 1999-439732 19991112 (9)
 RLI Continuation of Ser. No. US 1997-997195, filed on 23 Dec 1997
 Continuation of Ser. No. US 1994-315269, filed on 29 Sep 1994, now patented, Pat. No. US 5780225 Continuation of Ser. No. US 1992-919730, filed on 24 Jul 1992, now patented, Pat. No. US 5284555 Continuation of Ser. No. US 1990-464350, filed on 11 Jan 1990, now abandoned
 PRAI WO 1991-US209 19910110
 DT Utility
 FS GRANTED
 LN.CNT 1039
 INCL INCLM: 435/006.000
 INCL INCLM: 435/091.200
 NCL NCLM: 435/006.000
 NCL NCLM: 435/091.200
 IC [7]
 ICM: C12Q001-68
 ICS: C12P019-34
 EXF 435/6; 435/91.2; 536/22.1; 536/23.1
 CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 43 OF 48 USPATFULL
 AN 2001:163325 USPATFULL
 TI Nucleic acids encoding B7-1 and B7-2 molecules
 IN Sharpe, Arlene H., Brookline, MA, United States
 Borriello, Francescopaolo, Brookline, MA, United States
 Freeman, Gordon J., Brookline, MA, United States
 Nadler, Lee M., Newton, MA, United States
 Dana-Farber Cancer Institute Brigham, Boston, MA, United States (U.S. corporation)
 PA Women's Hospital, Boston, MA, United States (U.S. corporation)
 PI US 6294660 B1 20010925
 WO 9523859 19950908
 AI US 1997-702525 19970207 (8)

WO 1995-US2576 19950302 PCT 371 date
19970207 PCT 102(e) date
R1I Continuation-in-part of Ser. No. US 1994-205697, filed on 2 Mar 1994,
US 6218510
DT Utility
FS GRANTED
LN.CNT 2271
INCL INCLM: 536/023.500
INCLS: 536/023.100; 530/350.000
NCL NCLM: 536/023.500
NCLS: 530/350.000; 536/023.100
IC [7]
ICM: C12N015-12
EXF ICS: C12N015-11; C07K014-705
435/69.1; 435/70.1; 435/71.1; 435/172.2; 435/172.03; 435/243; 435/252.3;
435/320.1; 435/440; 435/455; 530/350; 536/23.1; 536/23.4; 536/23.5
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 44 OF 48 USPATFULL
AN 2001.163320 USPATFULL
TI Anti-interleukin-1 receptor antagonist antibodies and uses thereof
IN Ford, John, San Mateo, CA, United States
PA Pace, Ann, Scotts Valley, CA, United States
PA Hysed, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI US 6294655 BL 20010925
AI US 1999-417455 19991013 (9)
R1I Continuation-in-part of Ser. No. US 1999-348942, filed on 7 Jul 1999
Continuation of Ser. No. US 1999-287210, filed on 5 Apr 1999, now
abandoned Continuation-in-part of Ser. No. US 1999-251370, filed on 17
Feb 1999, now abandoned Continuation-in-part of Ser. No. US 1998-127698,
filed on 31 Jul 1998, now abandoned Continuation-in-part of Ser. No. US
1999-229591, filed on 13 Jan 1999, now abandoned Continuation of Ser.
No. US 1998-99818, filed on 19 Jun 1998, now abandoned Continuation of Ser.
US 127698 Continuation-in-part of Ser. No. US 1998-82364, filed on 20
May 1998, now abandoned, said Ser. No. US 9818 Continuation-in-part of
Ser. No. US 1998-82364, filed on 20 May 1998, now abandoned
Continuation-in-part of Ser. No. US 1998-79909, filed on 15 May 1998,
now abandoned Continuation-in-part of Ser. No. US 1998-55010, filed on 3
Apr 1998, now abandoned
DT Utility
FS GRANTED
LN.CNT 4656
INCL INCLM: 530/388.230
INCLS: 530/387.900; 530/388.100; 530/389.100; 530/391.100;
530/391.300; 530/350.000; 536/023.500; 436/501.000; 435/007.100;
424/134.100; 424/139.100; 424/141.100; 424/145.100
NCL NCLM: 530/388.230
NCLS: 424/134.100; 424/139.100; 424/141.100; 424/145.100; 435/007.100;
436/501.000; 530/350.000; 530/387.900; 530/388.100; 530/388.150;
530/389.100; 530/391.100; 530/391.300; 536/023.500
IC [7]
ICM: C07K016-18
ICS: C12P021-08
EXF 435/69.1; 435/69.7; 435/71.1; 536/23.5; 536/23.53; 436/501; 424/134.1;
424/139.1; 424/141.1; 424/145.1; 530/387.9; 530/388.1; 530/388.15;
530/388.23; 530/389.1; 530/391.1; 530/391.3; 530/350
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 45 OF 48 USPATFULL
AN 2000.171124 USPATFULL
TI Metal-regulated transporters and uses therefor
IN Gueriot, Mary Lou, Etna, NH, United States
Eide, David J., Columbia, MO, United States

PA Trustees of Dartmouth College, Hanover, NH, United States (U.S.
corporation)
Regents of the University of Minnesota, Minneapolis, MN, United States
(U.S. corporation)
US 6162900 20001219
US 1998-107858 19980630 (9)
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PRAI CA 1996-2187728 19960529 (60)
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DT Utility
FS Granted
LN.CNT 4260
INCL INCLM: 530/370.000
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ICM: C12N015-00
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CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 46 OF 48 USPATFULL
AN 2000.50562 USPATFULL
TI Receptor-mediated gene delivery using bacteriophage vectors
IN Larooca, David, Encinitas, CA, United States
Baird, Andrew, San Diego, CA, United States
Johnson, Wendy, Encinitas, CA, United States
PA Selective Genetics, Inc., San Diego, CA, United States (U.S.
corporation)
PI US 6054312 20000425
AI US 1997-920396 19970829 (8)
DT Utility
FS Granted
LN.CNT 2350
INCL INCLM: 435/320.100
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ICM: C12N015-63
ICS: C12N015-33; C12N015-12; C07K014-00
EXF 514/44; 435/320.1; 530/350; 530/387.1; 536/24.5; 536/23.5; 536/23.72
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 47 OF 48 USPATFULL
AN 1998.154133 USPATFULL
TI Metal-regulated transporters and uses therefor
IN Gueriot, Mary Lou, Etna, NH, United States
Eide, David J., Columbia, MS, United States
PA Trustees of Dartmouth College, Hanover, NH, United States (U.S.
corporation)
Regents of the University of Minnesota, Minneapolis, MN, United States
(U.S. corporation)
US 5846821 19981208
AI US 1996-758621 19961127 (8)
PRAI US 1996-18578P 19960529 (60)
DT Utility
FS Granted
LN.CNT 4077
INCL INCLM: 435/320.100

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NCL NCLM: 435/320.100

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536/024.100; 536/024.300; 536/024.310; 536/024.320; 536/024.330

IC [6]

ICM: C07H021-04

EXF 435/6; 435/69.1; 435/172.3; 435/320.1; 435/325; 436/501; 536/23.1;
536/24.1; 536/24.3-24.33; 935/77; 935/78

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L13 ANSWER 48 OF 48 USPTFULL

AN 1998:82528 USPTFULL

TI Method for generating libraries of antibody genes comprising
amplification of diverse antibody DNAs and methods for using these
libraries for the production of diverse antigen combining molecules

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DT Utility

FS Granted

LN.CNT 1174

INCL INCLM: 435/006.000

NCL INCLS: 435/069.100

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IC [6]

ICM: C12Q001-68

ICS: C12P021-00

EXF 435/5; 435/6; 435/91.2; 435/69.1; 435/69.7

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

Construction of combinatorial antibody expression libraries in *Escherichia coli*

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Abstract. A λ vector system has been developed for the construction and coexpression of diverse populations of heavy and light chain cDNA sequences. Heavy and light chain sequences within the immunological repertoire are generated by the polymerase chain reaction using primers directed to conserved regions within the variable region framework. Two λ vectors are employed for the independent construction of heavy and light chain cDNA libraries. The libraries are randomly combined to produce a population of λ phage with each containing one heavy and one light chain cDNA sequence. The vectors direct the synthesis and secretion of functional Fab antibody fragments from a dicistronic operon. Libraries of up to 1×10^7 recombinants can be obtained with a diversity approaching *in vivo* estimates. Analysis of the heavy and light chain combinations reveals that the complete antibody repertoire can be generated by subsequent reshuffling of heavy and light chain cDNAs within an initial Fab-producing library. Inherent bias found *in vivo* toward certain heavy and light chain combinations can be virtually eliminated.

1991 *Catalytic antibodies*. Wiley, Chichester (Ciba Foundation Symposium 159)
p 91-102

Monoclonal antibodies have been generated that catalyse a broad range of chemical transformations (Shokat et al 1989, Iverson & Lerner 1989). The rationale is to immunize mice with predicted transition state analogues in the hope that antibodies which bind the analogues specifically will function analogously to known enzymic mechanisms when presented with substrate. Apart from the unpredictable design of appropriate transition state analogues, the probability of finding antibodies where particular amino acid side chains participate in catalysis also depends on the number of different antibodies assayed.

Current methods for generating monoclonal antibodies do not provide an adequate survey of the natural immunological repertoire. For example, in an individual animal there are at least 5-10 000 different B cell clones capable of generating unique antibodies to a relatively small antigen (Schreier 1978, Lawrence et al 1973, Chiller & Weigle 1970). The *in vivo* process of somatic

mutation during the generation of antibody diversity additionally generates essentially an unlimited number of unique antibodies. In contrast, owing to the relative inefficiency of the *in vitro* process, the production of monoclonal antibodies generally results in only a few hundred different antibodies.

Successful expression of recombinant antibody molecules in bacterial systems has recently been accomplished (Skerra & Plückthun 1988, Better et al 1988). These prokaryotic systems satisfy all the criteria for assembly of functional antibody fragments. First, synthesis of approximately stoichiometric amounts of heavy and light chains can be accomplished by expressing both chains under the control of a single promoter. Second, transport of both precursor proteins to the periplasmic space occurs efficiently and accurately with correct processing of signal sequences. Third, recombinant antibody fragments are correctly folded into functional domains with correct disulphide bond formation. Fourth, heavy and light chain antibody fragments are self-assembled into functional heterodimers. Additionally, libraries have been constructed which express diverse populations of only heavy (V_H) chain polypeptides (Sasry et al 1989, Ward et al 1989). The antigen-binding affinity of single heavy chains for use as substitutes of Fab fragments is, however, one to two orders of magnitude lower than that of heterodimers. More importantly, heavy chains lose specificity because they tend to be sticky (Ward et al 1989).

The expression of antibody fragment libraries is an important extension of the recombinant expression of unique antibody species. Polymerase chain reaction (PCR) technology has allowed access to the diverse family of antibody genes via conserved sequences in the 5' and 3' portions of the variable, the framework and the constant region sequences. Specific amplification of antibody fragments using primers homologous to these conserved sequences allows the construction of libraries containing large populations of heavy and light chain antibody fragments. We report the use of λ phage libraries to generate diverse populations of functional Fab fragments. The system parallels the natural immunological repertoire, and reduces the inherent bias towards a small number of predominant species that is found within an *in vivo* population. Libraries can be constructed and screened for a desired antigen-binding activity in less than two weeks. This efficiency allows the rapid isolation of rare catalytic antibodies in a form suitable for genetic manipulation.

Results and discussion

To obtain a vector system for generating a large number of Fab fragments that could be screened directly, we constructed the expression libraries in modified bacteriophage λ expression vectors. Coexpression libraries are made by first producing separate heavy (V_H) and light (V_L) chain fragment libraries, then randomly combining the two libraries into a single vector population (Huse et al 1989). Each Fab fragment coexpressed from a single vector within the

dy diversity additionally generates antibodies. In contrast, owing to the production of monoclonal antibodies, the production of monoclonal antibodies in bacterial systems Plückhuhn 1988, Better et al 1988). criteria for assembly of functional proximately stoichiometric amounts of heavy chains under transport of both precursor proteins and accurately with correct processing antibody fragments are correctly folded and assembled into functional hetero-peptides (Sastri et al 1989, Ward et al 1989, Ward et al 1989). of single heavy chains for use as one to two orders of magnitude lower than in *in vivo* population. Libraries desired antigen-binding activity in less the rapid isolation of rare catalytic manipulation.

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Combinatorial antibody expression libraries

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randomly combined population retains all the characteristics exhibited by recombinant antibody fragments expressed singly. Moreover, random combination of both chains serves as a source of diversity and increases the total number of sequences which can be obtained.

The vectors used for expression of V_H and V_L sequences have been previously reported (Huse et al 1989) and are schematically represented in Fig. 1. Populations of V_L sequences are cloned into the λ light chain vector; V_H sequences are cloned into the λ heavy chain vector. The vectors are designed to be asymmetric with respect to the *NotI* and *EcoRI* restriction sites which flank the cloning and expression sequences. The asymmetric placement of these restriction sites in a linear vector allows the V_L -containing portion of the light chain vector to be combined with the V_H -containing portion of the heavy chain vector into a single linear vector for the coexpression of both chains. In addition to the asymmetric restriction sites, each vector includes a leader sequence for the bacterial *pelB* gene (Better et al 1988); a ribosome-binding site at the optimal distance for expression of cloned sequences; and cloning sites for either the V_L or V_H PCR products. The heavy chain vector contains a decapeptide tag at the C-terminus of the expressed V_H fragment for immunoadfinity purification (Field et al 1988).

For the synthesis of V_H and V_L sequences, polyA⁺ RNA is prepared from the spleen of a single immunized mouse and used in first-strand cDNA synthesis (Aviv & Leder 1972). Resultant DNA-RNA heteroduplexes are used as templates for subsequent amplification by PCR. Primers used for amplification of V_H and V_L sequences are as previously described (Huse et al 1989). V_H amplification is performed in eight separate reactions (Saito et al 1988) with each reaction containing one of eight 5' primers and a common 3' primer. The 5' primers incorporate an *XhoI* site in the PCR products and the 3' primer incorporates a *SpeI* restriction site. These sites are used for cloning the amplified products into the heavy chain vector in a predetermined reading frame for expression.

An analogous set of PCR primers is used for the amplification and cloning of mouse V_L sequences. These primers incorporate *SacI* and *XbaI* restriction sites into the PCR products for orientational cloning in the correct reading frame. PCR is performed in independent reactions using five separate sets of primers to ensure unbiased amplification of mRNA sequences. Each reaction contains one of the five 5' primers and a common 3' primer. PCR products are pooled and cloned into their respective vectors for the construction of separate V_H and V_L libraries.

The heavy chain library was created from mRNA isolated from the spleen of a 129G1x mouse previously immunized with a *p*-nitrophenyl phosphonamide transition state antigen (NPN) coupled to keyhole limpet haemocyanin. This primary library contained 1.3×10^6 plaque-forming units (pfu) and at least 80% of the clones express the Fd fragments when assayed by

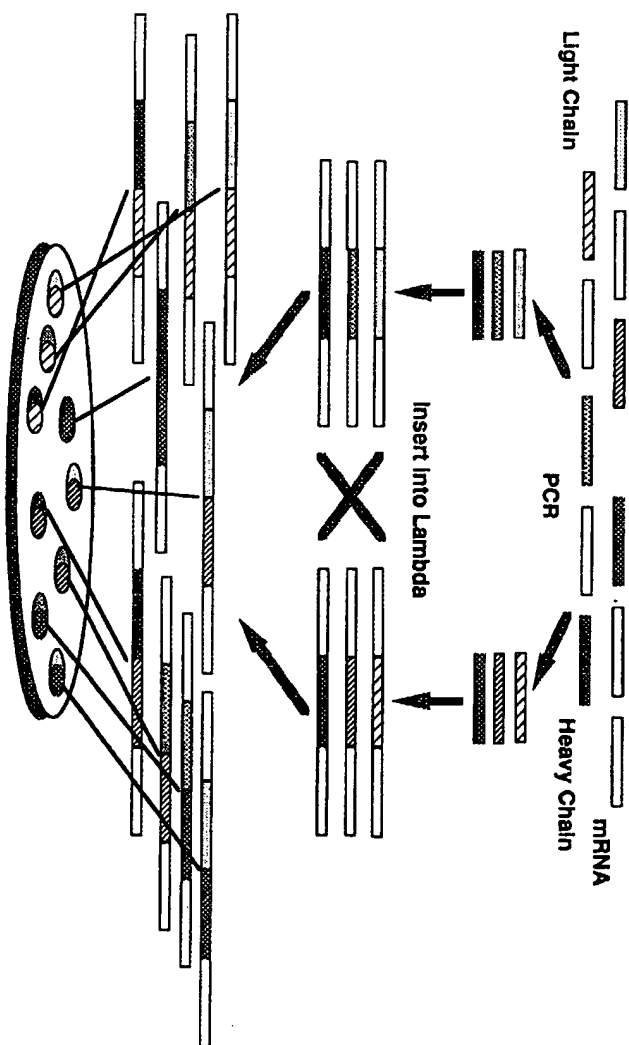


FIG. 1. Scheme for cloning V_H and V_L sequences into λ vectors then crossing the vectors to give coexpression of both chains in a single linear vector.

immunodecison of the decapeptide tag. The light chain library was constructed in an identical fashion and shown to contain 2.5×10^6 members. Screening with an antibody to κ chain indicated that 60% of the library expressed light chain inserts.

A single Fab expression library was constructed by ligating the left λ arm containing V_H sequences to the right λ arm containing V_L sequences from each library. To create the library where each vector coexpresses a single heavy and a single light chain-encoding sequence, we performed step-wise restriction of the separate library DNAs to eliminate the λ arms not carrying either encoding sequence. Therefore, the only products which can join together to produce viable phage are the arms containing the heavy and light chain sequences. Light chain library DNA is first digested with *MluI*. The ends are dephosphorylated and then digested with *EcoRI*. Preparation of heavy chain library DNA is performed analogously, however the first digestion is with *HindIII*. Products are ligated at their *EcoRI* sites to create a coexpression library.

Reverse immunoscreening of one million phage plaques with labelled NPN coupled to bovine serum albumin (BSA) identified approximately 100 clones which bound to antigen. Antigen-antibody specificity was determined for five of the clones by competition with free unlabelled antigen. The results demonstrated that individual clones could be distinguished on the basis of antigen-binding affinity; the concentration of free antigen for complete inhibition ranged from 10 to 100×10^{-9} M. They also show the production of a recombinant antibody library which compares favourably with the *in vivo* repertoire in terms of size, diversity and antigen-binding affinities.

The mammalian repertoire is typically estimated to contain 10^6 to 10^8 different antigen specificities. Antibody libraries of this size can be obtained using standard recombinant methods and screening techniques to access this number of different molecules in a relatively short time. If more diversity is needed, heavy and light chains within the initial coexpression library or from the original single chain libraries can be systematically shuffled to give larger libraries. Reshuffling of heavy and light chains allows the generation of virtually all possible combinations of V_H and V_L pairs, since the number of individual chains within the library is smaller than the number of possible pairs. V_H and V_L chains can be represented as components of a grid (Fig. 2), with V_H chains along the top row and the V_L chains down the side column. Pairing each chain in a row with each in a column produces a matrix containing all possible combinations (Fig. 2, top). This matrix can be viewed as the total immunological repertoire within an organism. If the initial library does not contain all possible combinations but has each heavy and light chain represented in the population (Fig. 2, middle), then the entire matrix can be generated by reshuffling the chains. The three matrices in Fig. 2 (middle row) represent recombinant antibody populations which might be obtained after the initial construction of the library.

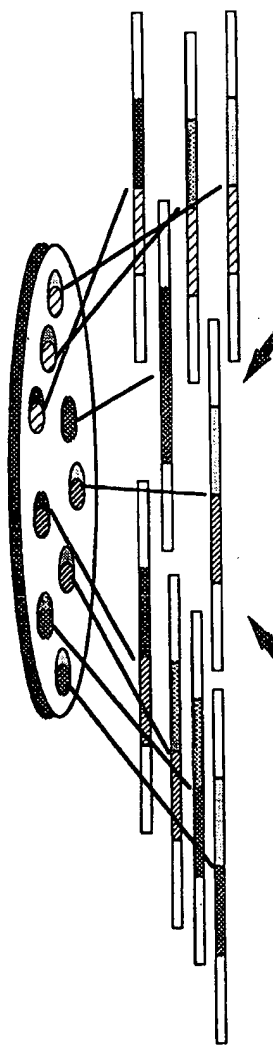
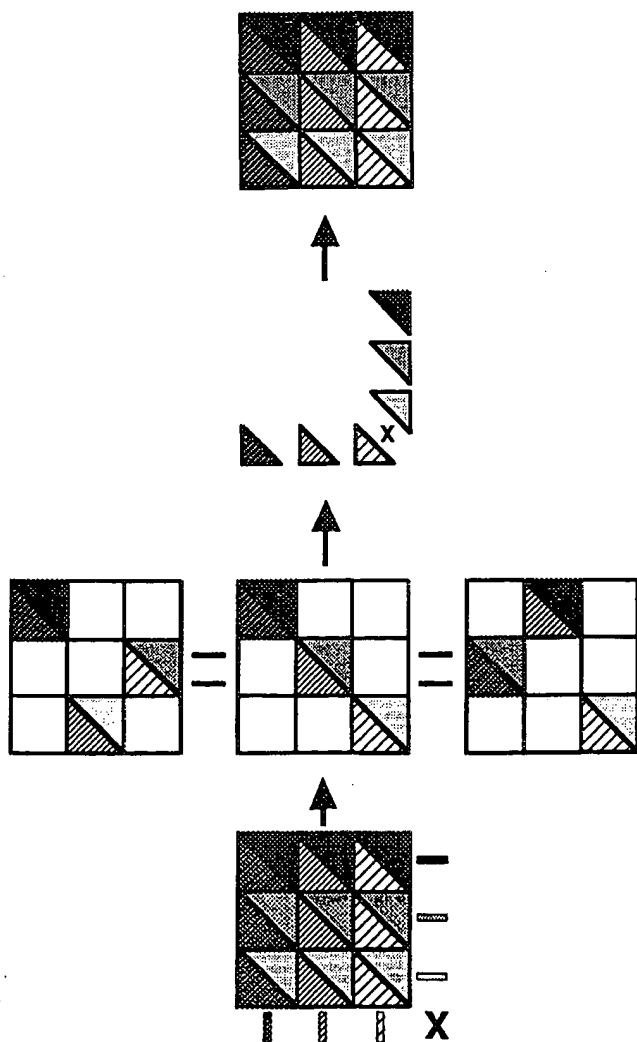


FIG. 1. Scheme for cloning V_H and V_L sequences into λ vectors then crossing the vectors to give coexpression of both chains in a single linear vector.

FIG. 2. Schematic representation of the way in which the complete immunological repertoire of an organism can be obtained from individual libraries that contain different subsets of heavy and light chain sequences.



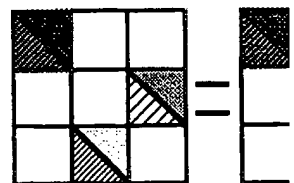
Recombinant antibody libraries also create a relatively unbiased distribution of possible species within the population. Inherent within the immunological repertoire will be prevalence of certain species because of factors such as favoured heavy and light chain re-arrangements and selection of particular heavy and light chain combinations by immunization of the animal. The *in vivo* repertoire has been modelled to account for these factors. Shuffling of the predominant heavy and light chains with the less prevalent chains produces a new population with different characteristics. Diversity within the population does not change, but the frequency of individual species is more equally represented. Unbiased representation of all possible species allows easy access to many more rare antibody species than could previously be obtained.

These results demonstrate that it is now possible to construct and screen several orders of magnitude more clones than using standard immunological techniques. Given the characteristics of recombinant libraries, it may now be possible to isolate antibodies to any desired antigen without immunization of live animals.

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y in which the complete immunological individual libraries that contain different three matrices are equivalent in that y unliking heavy and light chain pairs ate the complete repertoire of possible nt libraries can be constructed which : of the natural immunological system.



DISCUSSION

Schultz: The primers you used have 80% homology with framework 2 sequences from the Kabat sequence collection. When we use those primers we get mis-priming in framework 2.

Huse: Is the homology with framework 2 of the heavy chain or the light chain? **Schultz:** Both. In many of our PCR reactions we see two bands on the gel and one must be careful to choose the right band.

Kang: Dennis Burton and I have sequenced a group of mouse and human immunoglobulin variable regions generated by PCR using primers designed to amplify sequences from framework 1. In the case of mouse Fabs that bind NPN-hapten, we have sequenced V_H and V_L for 20 individual clones and have sequence for framework 1 of the heavy and light chains, respectively, for each one. Dennis Burton has observed the same for human V_H and V_L regions.

Huse: We have sequenced 25 randomly chosen clones. All those clones contained framework 1 sequences.

Burton: The upper bands are much higher on the gel. I am surprised if that's true in the sense of putting the decapetide in frame.

Huse: From the homology of the amino acid sequences, you would expect the decapetide to be in frame.

Schultz: We also get the decapetide in frame. I have a compilation of the primers and the matches. In every case there is only a 2 bp mismatch. There is also a third reading frame containing a *lacZ α* insert. Would that contribute to the translational inefficiency?

Huse: I wouldn't doubt it. It is difficult to get rid of that site in λ phage. It is very cumbersome to construct anything in λ phage. We are now making some new vectors that will not have that *lacZ* insert.

Shokat: This library is from a mouse immunized with a keyhole limpet haemocyanin (KLH) conjugate. Have you tried screening the light chain library and the heavy chain library separately against a KLH plate?

Huse: We did not test these specific libraries with KLH, but we did test some earlier ones. The problem is that KLH is sticky and when you get spots they don't replicate very well.

Shokat: Could you get heavy chain binding in the absence of light chains, or vice versa?

Kang: We screened the combinatorial library generated from mice immunized with NPN-KLH and found that the KLH sticks to everything. We have no evidence that heavy or light chains alone bind to NPN-bovine serum albumin.

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Lerner: Caion & Koprowski (1990) have made a library to influenza virus
antigen by hybridoma technology and basically got the same antibodies. They
then screened the heavy and light chains individually and did not get any binding.

Paul: That would be a function of binding affinity.

Huse: Binding below a certain affinity (I am not sure what that affinity is)

would not be seen using this assay.

Paul: If the assay could detect interactions with weaker affinities, presumably
you could pick up binding by single chains.

Huse: The question is, when you do find something that sticks to the heavy
chain alone, is that binding specific? If it is not specific, is it predictive of a

heavy chain that in combination with a particular light chain will confer
specificity? I do not believe the heavy chains that bind non-specifically alone
will, in combination with any light chain, necessarily become specific for an

antigen.

Mountain: Can you manipulate the stringency of the probing to select for
high affinity antibodies?

Huse: I would imagine so, but I don't know. The assay is probably not that

sensitive. The concentration of the antibody is not well controlled in those A
phage plaques; different plaques may have very different levels of antibody
expression, which will make it hard to separate differences in expression levels

from differences in affinity.

Mountain: What's the evidence that you need a bicistronic arrangement of
the heavy and light chain gene sequences?

Pluckhuhn: We have used the bicistronic construct, but have also used two

different plasmids: the bicistronic construct is the most efficiently repressed.
This is important as the induced cells start to lyse. I don't think there is an
intrinsic physical reason why the information for both protein chains would

have to be on one mRNA molecule.

Mountain: It is not to do with heavy and light chains needing to be secreted
in close proximity?

Pluckhuhn: I don't think so. Secretion and folding in each other's presence
are what is required, but I don't think that the proteins know whether they were
coded on one or two mRNA molecules.

Paul: Dr Huse, the primers you used for amplification by PCR are derived
from the amino acid sequences of a limited number of antibodies. Will these
primers lead to amplification of every antibody cDNA or nearly every one?

Huse: This method will lead to isolation of the heavy chains that are normally
present in the response of a mouse. Dennis Burton and Andreas Pluckhuhn can
say more about the diversity of the sequences that are isolated in terms of
antibodies to a particular antigen. If we are generating a very diverse set of
antibodies to a particular antigen, that would suggest that PCR priming occurs

fairly universally on antibody sequences.

Burton: The impression is that you are getting an extremely large, diverse library. That could be true for non-immunized animals, but in an immunized animal, presumably the levels of mRNA from the immunized B cells are much greater, so the repertoire of antibodies generated is limited. Caton & Koprowski (1990) found that one in 200 heavy chains were identical. In the mouse the number of binding sequences is limited: in humans it is greater but still limited. As Richard Lerner has said, the hybridoma technology gives a limited number of sequences.

Plückhuhn: How do you check the diversity of your plaques? **Huse:** From the initial library made with these PCR primers we sequenced 25 randomly chosen clones and they all had different sequences. 20–25% had only a few base pairs different; others had very unrelated sequences. **Hilvert:** Gene recombination events are likely to be independent of protein structure, but there might be a structural bias against certain combinations of different heavy chains with different light chains. Is that ever seen in structures of antibodies? Are there certain classes of combinations?

Plückhuhn: This has been argued for a long time, but there are only a few well designed experiments that address this question. For the different types of phosphorylcholine-binding antibodies, you can obtain cross-association, but you get no antigen binding by any of the cross-associated molecules, only by the original ones. Only in some cases can we understand structurally why the antigen is not bound.

Hilvert: But do you get stable heavy and light chain dimers in the case of the non-binders?

Plückhuhn: That was what was reported by Hamel et al (1986). **Burton:** We have seen the same heavy chain pair with different light chains and still give binding.

Huse: But a heavy chain that binds with more than one light chain still does not bind antigen when combined with most available light chains.

Lerner: If you mutate the framework regions of the antibodies, you get individual specificities. People would argue that in the very high affinity antibodies, not only have you mutated the loops, you have also mutated the dimer interface. Those structures that don't fit any longer drop out. The people who study this effect would argue that private associations occur in less than 5–10% of the very high affinity antibodies. **Hansen:** Are any of the antibodies that you raised against the transition state analogue catalytic?

Janda: The problem is that not much protein is produced. Although several different reactions have been catalysed by antibodies, most of the reactions require large amounts of antibody (e.g. 5–20 μ M). We have begun to screen some of the antibodies from the library to the nitroanilide phosphonamide. We began with 20 and have identified one tentatively that cleaves the ester but not the anilide. It must be different from antibody 43C9 because the latter cleaves

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both the anilide and the ester. We have the DNA sequence of each antibody, so we can see the differences between them.

Hansen: Have you made a library against a transition state analogue that gave a much higher hit rate in the traditional immunization procedure? By traditional immunization, this analogue yielded one catalytic antibody out of 50 you studied; if you are seeing zero out of 20 that could be consistent with the numbers you had before.

Janda: The idea was that by using the library we could find a much greater number of hits.

Schultz: When you screen against that particular hapten for catalysis, won't you run into problems with bacterial enzymes?

Lerner: You can't screen plates for ester and amide hydrolysis. We've tried periodically to screen for substrates in the agar but the bacterial lawn alone often causes the plate to change colour.

Schultz: We're looking at using D esters or amides to do these screens.

Huse: The underlying question is the desirability of doing the assay for catalysis directly without screening for binding initially.

Janda: You would have to have an antibody with a huge turnover number. **Schultz:** Or an extremely sensitive assay. We have built into our hapten a fluorescence energy transfer assay which is extremely sensitive.

Lerner: Phage plaques are often screened by enzymic assay, for example the release of halogenated indoles, but β -galactosidase is a very efficient enzyme. **Jencks:** Do you have a rough estimate of the affinities of the heavy and light chains compared to that of the intact molecule?

Huse: We don't see anything with the heavy and light chains separately. **Lerner:** The problem with heavy chains is they like to stick to things, including light chains and plastic. It is very difficult to study heavy chains alone.

Plückhuhn: We find exactly the same thing, both the V_H domain alone and the whole heavy chain of the Fab fragment have real problems with solubility. Therefore I am sceptical at least about the generality of using these as antibody substitutes. I don't want to deny that it may work in some cases, but if it's not general, it may not be so useful.

Lerner: The only formal experiment that has been done is that of Andrew Caton. He made a library to a protein molecule, not a small hapten. He divided the library in half and did not see any binding. He could have had, according to the DNA sequences, one in 200 of the heavy chains as proper binders but looking at a million he didn't see any.

Huse: One reason for looking at heavy chains alone was that it was not possible to look at the heavy and light chains together. Hopefully, that is not going to be an issue in the future.

Paul: I am having difficulty relating this discussion to work done in the 1960s and early 1970s. The antibody paratope is a complex of V_H and V_L . Dissociated antibody chains could possess either reduced or no antigen binding

activity. It was shown by immunochemical methods that single chains can bind antigen: heavy chains were found to bind better than light chains (Franek & Nezlin 1963, Porter & Weir 1966, Utsumi & Karush 1964). More recently, Greg Winter and co-workers showed that recombinant V_H binds lysozyme (Ward et al 1989). The single chains have reduced binding affinity, but there is little doubt that it is true binding rather than non-specific 'stickiness'.

Huse: The two cases are different. In the first, you take antibodies that bind antigen and ask if their isolated heavy chains have any residual affinity. In the second, you take isolated recombinant heavy chains that stick to an antigen. One would like to know if these are the same population as in the first case. I believe the isolated heavy chains in the second case are probably ones that had residual affinity in the first case plus a bunch of others that are just plain 'sticky' and have nothing to do with specific antibodies. This 'stickiness' could give a background signal that overwhelms the small signal from the residual affinity of heavy chains in the first case.

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and Richard A. Lerner

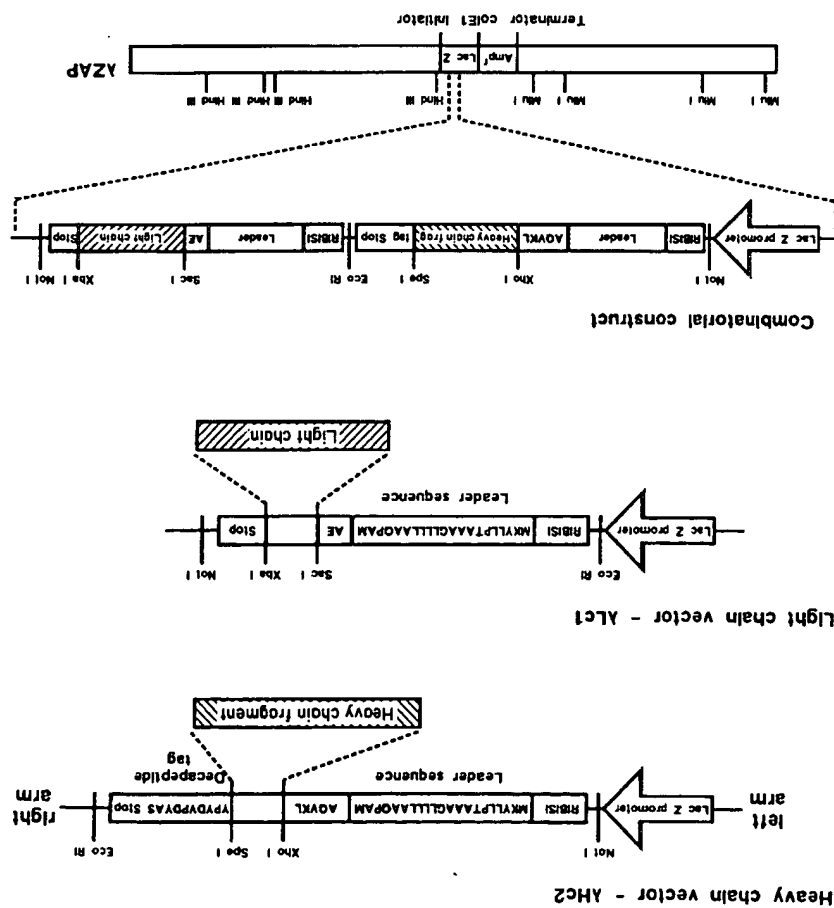
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Abstract. A bacteriophage λ vector system for the expression of Fab fragments from the mouse antibody repertoire in *Escherichia coli* has been described. We have used this system to generate a catalytic antibody from a combinatorial antibody library. Monoclonal antibody 43C9 was raised against a transition state analogue of the hydrolysis of carboxyamide. mRNA from hybridoma cells expressing this antibody was cloned into phage λ and clones that expressed the mRNA for either the heavy or the light chain of the antibody were isolated. These individual libraries were then crossed to generate a combinatorial library in which clones coexpressed the heavy and light chains. This library was screened for antibodies/Fab fragments that bound to the original antigen with high affinity. A sequencing showed that these fragments were the same as those in antibody 43C9. Three different clones were found to catalyse the hydrolysis of carboxyamide. More efficient expression vectors and improved screening techniques should lead to the isolation of many more catalytic antibodies from combinatorial antibody libraries.

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FIG. 1. Combinatorial bacteriophage λ vector system for expression of Fab antibody fragments. The LC1 vector is for cloning PCR products of mRNAs that code for κ light chains; the HC2 vector is for cloning PCR products of mRNAs coding for heavy chain Fd sequences. The combinatorial constructs that can express Fab fragments are generated by cutting light and heavy chain DNA at the antisymmetric *EcoRI* site of each vector, followed by religation of the resulting arms.

for surveying the immunological repertoire and limits the number of catalysts that can be obtained. We have developed a system using bacteriophage λ to clone and express a combinatorial library of Fab fragments of the mouse antibody repertoire in *Escherichia coli* (Fig. 1) (Sastry et al 1989, Huse et al 1989). The system allows rapid and easy identification of monoclonal Fab fragments in a form suitable for genetic manipulation. However, it remains to be shown that such combinatorial libraries can be used to produce catalytic Fab



fragments. In this paper we demonstrate the generation of a catalytic antibody from a combinatorial antibody library.

Using the λ phage system we generated an Fab combinatorial library from the spleen of a mouse immunized with phosphonamide 1 (NPN), a transition state analogue for the hydrolysis of carboxamide substrate 2 (Fig. 2). Screening the library with the antigen, NPN, linked to bovine serum albumin (NPN-BSA) resulted in the identification of a number of Fab fragments that bound to the antigen in a competitive manner. To find efficient catalysts for the hydrolysis of the nitroamide 2, we screened the Fab combinatorial library directly for catalysts. The induced phage libraries were incubated with nitrocellulose filters saturated with the substrate, or the substrate was added directly to agar containing cells infected with the phage before they were poured onto a plate. Unfortunately, these approaches were unsuccessful because of the chemical nature of the reaction as well as the limited amount of Fab that is secreted by the phage molecules. It has previously been observed that catalysis of hydrolysis of the amide 2 occurs at 37 °C with high concentrations of an antibody (Janda et al 1988). The high concentrations of antibody required for catalysis are difficult to achieve directly on the phage surface. Also, the product of the hydrolysis, *p*-nitroaniline, is diffusible and is hard to observe either directly on phage

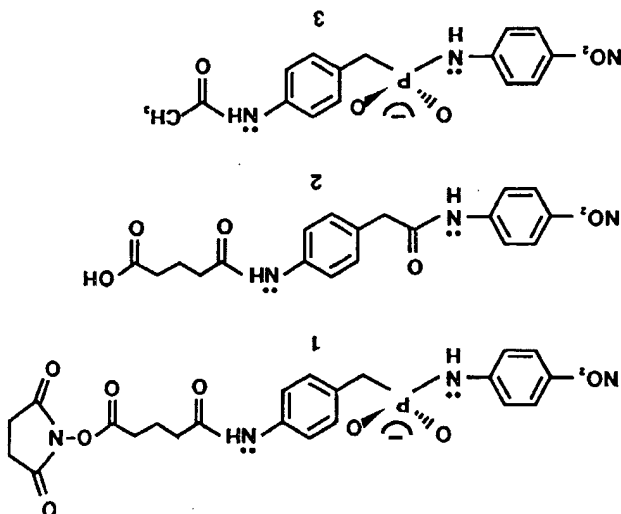
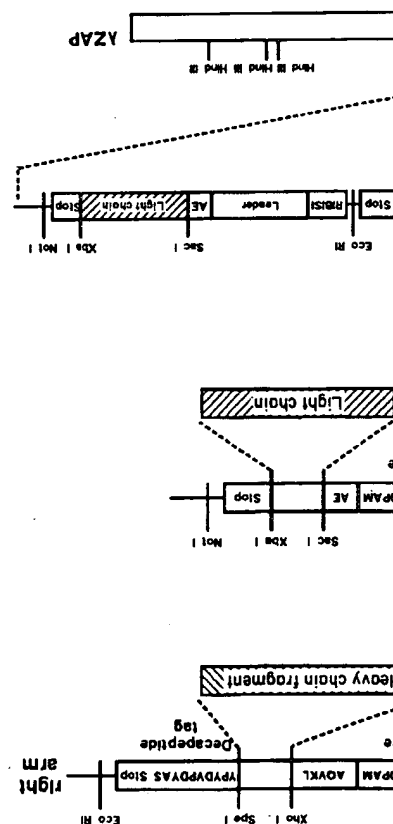


FIG. 2. The transition state analogue phosphoramidate **1** (NPN) which was used to induce antibodies that hydrolyse the carboxamide substrate **2**. The phosphoramidate functionality mimics the stereoelectronic features of the transition state for hydrolysis of the amide bond. The transition state analogue **3** is an inhibitor of the reaction.



A system for expression of Fab antibody products or mRNAs that code for light chains of mRNAs coding for heavy chain can express Fab fragments are generated asymmetrically at site of each vector.

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plaques or on nitrocellulose filters. Because of these practical limitations, we decided to screen initially for Fab fragments that bound to NPN and then for those that showed catalytic activity. As an essential first step, we cloned and expressed a monoclonal antibody (43C9) that catalyzes the amide hydrolysis in the phage system (Janda et al 1988). Besides being an internal control, the expression of the monoclonal antibody in phage also allows the study of its structure and mechanism of catalysis. Mutagenesis and chain-exchange experiments can be easily performed on the cloned antibody to improve its catalytic activity.

Methods

Total RNA from 10⁷ 43C9 hybridoma cells was isolated as described (Chomczynski & Sacchi 1987). The mRNAs were purified on an oligo dT column, then amplified using the polymerase chain reaction to obtain separate pools of heavy and light chain DNA (Sastry et al 1989, Huse et al 1989). Amplification of heavy chain DNA was performed with eight different 5' primers and a 3' primer specific for the IgG2b isotype. Light chain DNA was similarly amplified with five 5' primers and a κ chain-specific 3' primer. Heavy and light chain libraries were generated in phage λ and crossed to obtain an Fab combinatorial library (Huse et al 1989). This library was then screened with NPN-BSA labelled with ¹²⁵I and Fab fragments that bound the antigen were identified (Huse et al 1989). These Fab fragments were excised using helper phage (M12 mp8) and McBlue cells and plated on LB/ampicillin plates (Short et al 1988). Colonies on the plates represented the excised plasmid carrying the cloned heavy and light chain pieces.

Individual clones were grown up and their protein products isolated using an affinity column made from anti-(Fab')₂ coupled to Sepharose beads. Purified Fab was dialysed for 4–6 hours against ATE (Acces, Tris, ethanolamine) buffer, pH 9.0, concentrated to 1–3 μM solution, and used for catalysis. Catalysis was performed at 37 °C in ATE buffer at pH 9.0 with the 1–3 μM Fab solution and a saturating amount (1 mM) of substrate 2. Sequencing of the positive clones was as described by Sanger et al (1977).

Results

PCR amplification of heavy and light chain DNA resulted in bands of about 700 bp as analysed by agarose gel electrophoresis. A number of different primers were used for amplification from the hybridoma cells, because these may contain other non-functional heavy or light chains and restricted amplification may result in the cloning and expression of the wrong chains. To avoid this problem, we pooled the amplified DNA from the heavy and the light chains, then cloned each pooled fraction into the expression vector. Cloning of heavy chains resulted in 2 × 10⁶ recombinants; the light chain library contained 5 × 10⁵ recombinants.

Screening of the heavy chain recombinants with an antibody raised against a conserved 10 amino acid sequence in the heavy chain showed that 90% of these were expressing the decapeptide and therefore the heavy chain. Anti-k antibody screening of the light chain library indicated that 60% of the clones were expressing k light chains. The combinatorial library consisting of 2×10^7 recombinants was screened with the anti-decapeptide and anti-k antibodies; 65% of the clones coexpressed heavy and light chains.

The Fab library (3000 plaques/plate) was then screened with iodinated NPN-BSA and positive clones were identified after a three-day exposure. Fragments that bound the antigen (binders) were identified at a frequency of 1/200; this relatively low frequency may be due to the presence of non-functional heavy and light chains in the Fab library. Ideally, amplification of the hybridoma RNA with specific 5' heavy and light chains should generate Fab fragments that bind at a much higher frequency.

The DNA sequences of the binders were obtained to identify the clone that exactly represents the monoclonal catalytic antibody 43C9. Comparison of the light chain deduced N-terminal amino acid sequence of antibody 43C9 and the deduced amino acid sequences of ten of the binders indicated that five of the clones (8a11, 8a12, 8a1, 7a2, 7a4) had the correct light chain. Three of these clones (8a1, 8a11, 8a12) were identical and differed from each of the other two (7a2, 7a4) by a single amino acid in the framework region. All the clones had the same heavy chain sequence; comparison with the N-terminal sequence of the authentic antibody was not possible because its N-terminus is blocked.

Purified Fab from each of the ten clones described above was assayed for catalytic activity; 8a11, 7a2 and 7a1 hydrolysed amide 2 at a rate clearly above the background rate (Fig. 3). The reaction was inhibited completely by the addition of transition state analogue 3, 20 μ M. This indicated that the observed catalysis was exclusively due to the Fab. SDS-PAGE of the catalytic recombinant Fabs showed a single species at 50 kDa. Reducing conditions gave a doublet at 25 kDa, indicative of a single pure Fab fragment. Because of the limited amount of Fab produced in our system, detailed kinetic analysis has not been possible. Overexpression of the catalytic Fab is currently being sought, to facilitate the kinetic studies.

Discussion

The bacteriophage λ vector system developed for the expression of Fab fragments is ideally suited for studying the structure and mechanism of any desired monoclonal antibody. We have successfully expressed a monoclonal catalytic Fab in this system and have shown that it retains the ability to catalyse a specific amide hydrolytic reaction.

Future studies will be aimed at identifying more binders from the library which also display catalytic activity. The success of these will hinge upon our ability

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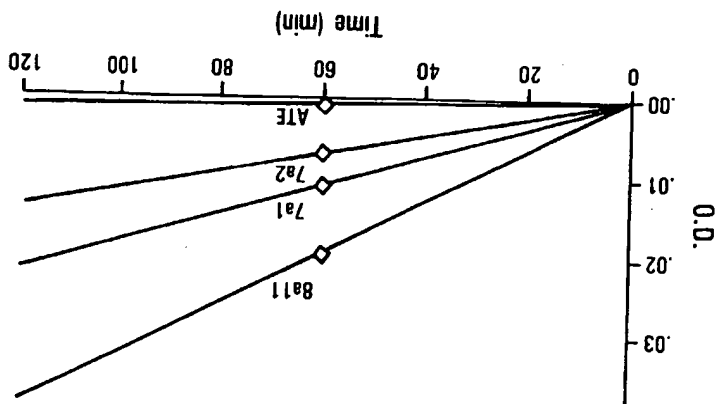
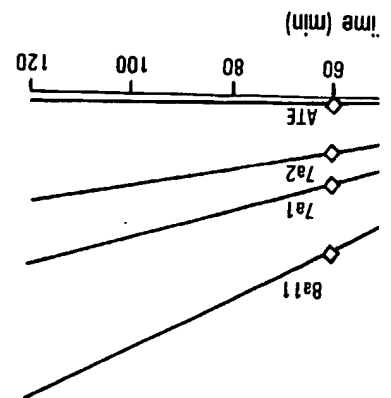


FIG. 3. Hydrolysis of carboxyamide 2 by Fab clones 8a11, 7a2 and 7a1. Hydrolysis was carried out at 37 °C with 2 μ M antibody, 1 mM substrate in ATE buffer, pH 9.0. The differences in the observed rates seen for each clone probably reflect inaccuracies in protein concentration determination rather than clone differences. The background hydrolysis was measured with the substrate alone; in all cases the reaction was monitored at 405 nm.

to obtain a better system for expressing the protein, possibly utilizing Summer's baculovirus system (Smith et al 1983). More efficient screening for catalytic antibodies might be achieved via a genetic selection process. Finally, a general solution to the antibody catalysis of a peptide bond may be obtained using the phage technology presented. Recently, we have constructed a single chain antibody with a coordination site for metals (Iverson et al 1990). When this site is incorporated into the light chain of an Fab fragment, a bound metal ion could act as a hydrolytic cofactor when properly aligned with a heavy chain which binds a small peptide sequence. The possibility of such a reaction appears remote; however, by taking advantage of the large numbers and combinations available through the combinatorial library, opportunities for success are within reach.

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Hansen: The exact placing of an amino acid is critical for enzyme catalysis. Do you have a sense, perhaps from Sargeson's work (Buckingham et al 1970), of how precise one has to be in orienting a carbonyl group near the metal ion to see catalysis?

Lerner: I don't know. They were basically looking at an intramolecular situation, because the substrate was directly bound to an open site on the coordination complex.

Martin: Another structural detail to consider is the geometry of the antibody's metal-binding ligands. A slight difference in the relative positions of metal-binding amino acid side chains could have a dramatic effect on the catalytic efficiency of the antibody. The coordination geometry of metals in natural enzymes is often distorted: for example, the tetrahedral geometry of cobalt-substituted carboxypeptidase A is markedly irregular compared to simple tetrahedral complexes of cobalt such as cobalt tetrachloride. In their entatic state hypothesis, Vallee & Williams (1968) proposed that the distorted coordination geometry is a critical feature of metalloenzymes in that it causes the metal to be unusually reactive—in their terms 'poised for catalysis'.

Lerner: Isn't that flying in the face of results from a great number of coordination complex experiments?

Jencks: Ground state strain of that kind can change the properties of the ions and the ligands and the metal, certainly; but to say that the ground state strain or distortion directly influences the transition state is wrong. It may provide a system which has a proper pK or oxidation potential or whatever, that will lead to a transition state more readily, and this might be done better with another metal that has a different size and a different potential, but it doesn't relate directly to the stability of the transition state.

Martin: If the enzyme or antibody binds a metal with tetrahedral geometry, say by three amino acid side chains and a reactive water molecule, the effect of the distorted coordination geometry might be to fine tune the pK of the metal-bound water molecule, thereby making it more reactive.

Hansen: In the crystal structure of the metalloantibody (Iverson et al 1990), are there any peptide bonds of the antibody itself near the metal ion which might cause autodecomposition?

Lerner: We tried to do that experiment with copper(II). We think we have seen rather restricted proteolysis, but that uses other copper coordination sites outside the binding pocket of the antibody.

Plückhuhn: Have you looked at the effect of the presence of the metal ion on the folding of the protein?

Lerner: Yes. The protein can re-fold with and without the metal.

Plückhuhn: Are you surprised that the metal gets in and out so easily?

Lerner: No; it does so in enzymes. We were careful to do the whole experiment in metal-free water, because we didn't want any extraneous metals to get into the site.

Schultz: There is a phenolic oxygen fairly close to the metal ion in the antibody combining site. Have you looked at hydrolysis of fluorescein esters?

Lerner: No.

Iverson: We tried fluorescein diacetate and obtained no rate enhancement for the hydrolysis of this compound by the antibody in the presence or absence of the metal.

Lerner: But in terms of other partners for coordination, which Peter Schultz is asking about, there is another possibility, namely an aspartate that could be a coordination partner.

Suckling: Have you looked for electron transfer reactions in any metalloantibodies?

Lerner: Not yet, but we hope to.

Willson: Have you tried a general screen with peptides to see whether any other antigens bind, as Scott & Smith (1990) did?

Lerner: No; it would be very interesting to do. Raymond Dwek's lab found a metal-binding site in a known antibody. If one is interested in accidents, one ought to screen catalytic antibodies, plus and minus metal. But metals can also make enzymes function considerably worse!

Jencks: I suspect you have thought of a good many things that metals will do, when they are attached to antibodies. Would you say any more on what you think about doing in the future?

Lerner: We plan to try to solve the so-called 'pre-mnonsin syndrome', which means how many chemist man hours are required to make monensin from pre-mnonsin, the problem being that there are so many chemically identical alkenes. We want to selectively epoxidize those molecules to do stereochemistry. We also, like Peter Schultz, want to try oxygen transfer reactions, particularly hydroxylation of steroids.

There are two important things to be done. One is to use these metalloantibodies for asymmetric inductions, where one would not have to use chiral auxiliaries because the antibody would give the system its asymmetry.

The success of that approach depends on (1) the binding specificity, and (2) how much trouble we shall have when we use relatively strong reagents like peracids.

Secondly, the single most important experiment one could do, thinking of the medical applications, is the selective cleavage of peptide bonds, using a recognition unit of seven amino acids rather than one or two. Proteases are relatively promiscuous enzymes and depend in part on the site environment rather than on the sequence of amino acids. One could not inject trypsin, for instance, into a person because it's too promiscuous. The ability to position ZnOH selectively in relation to seven amino acids would be tantamount to developing a restriction enzyme for protein molecules.

Benkovic: We also provide spectroscopists with a chance to investigate copper environments. There is a scarcity of models for copper(I) and copper(II) in various binding sites: by having a system that we shall be able to characterize by X-ray crystallographic analysis and manipulate at will, we should obtain interesting spin echo and electron paramagnetic resonance spectra for copper in these kinds of sites.

Lerner: If one is also interested in the flight of the electron in the protein cavity, there is no reason why one couldn't put two metals in there at defined distances and measure the rates of electron transfer.

Schultz: Could one use metal ion detoxification (such as HgII resistance) as the selection pressure to induce antibodies that have a metal-binding site?

Lerner: I think so. People have similar concepts to what you are talking about for immunization with alkylating agents: what if you were to immunize with a compound containing an open coordination site, such as HgII?

Hansen: The prospect of peptidases with more restricted recognition sites is very exciting. On a specific point, where is the metal ion in relation to the seven amino acid binding cleft that you mentioned?

Lerner: I don't think one can generalize about this. Because Ian Wilson is our neighbour, we have looked very closely at what we could do to cut a peptide in complexes whose structure he has solved. I don't believe a metal site would be close enough to any of the peptides that he has in his X-ray crystal structures to deliver the hydroxyl group effectively.

Hansen: The reverse question is whether the metal site would block peptide binding.

Lerner: If you look at the site in a 'cut-away' view, and if you assume that the peptide goes into it like a straight molecule, which it probably does not, it would not be easy to approximate a scissile bond, let's say next to a ZnOH . So you might wish to go further up the site. An antibody molecule often has a groove that could accommodate a peptide. I can imagine that the peptide will lie in that groove and approximate a scissile amide to the zinc ion. However, it remains to be shown that the present construction is good for peptide bond cleavage.

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Hansen: Is the binding constant such that the metalloantibody holds together at zero metal concentration?

Lerner: The formation constant for CuII is micromolar. The constant for zinc is unknown.

Hansen: What about using a metalloantibody *in vivo*, therapeutically?

Lerner: At the moment one would have to pre-load. If the disease you want to cure is critical, you could infuse both the antibody and the zinc into the patient to increase the *in vivo* concentration of zinc. You could not do this with copper or other more toxic metals.

We hope soon to finish the coordination chemistry of the L-I-L3 site, where we have tried thiols and carboxylates. I would be pleased to get a coordination constant of 10^8 - 10^9 there. There are many permutations of those three side chains that one needs to look at.

Harris: Many proteins have calcium associated with them. Have you thought about trying to introduce calcium-binding sites into antibodies?

Lerner: Steve Benkovic pointed out to me that when a protein binds carboxylates it tends to use calcium. It's very difficult to make an antibody with a good binding constant for carboxylate. Elvin Kabat said that he had never seen one better than millimolar. So to build an antibody that binds a carboxylate, one might do as you suggest.

Harris: Calcium binding occurs via aspartate residues: where would be the best site for those to be placed?

Lerner: We are making 3-Asp and 3-Glu sites to see how those work.

Paul: You mentioned that R. Dwek's group had a monoclonal antibody with a metal-binding site, is it known where the metal is bound?

Janda: R. Dwek and co-workers found that the MOPC315 antibody bound lanthanides (Dower et al 1978). The antibody was pretty well characterized by Steve Dower (1978). He found that two carboxylates bound a lanthanide in addition to binding a *p*-nitrophenyl phosphate as a reporter molecule.

Burton: I wonder if you should make so much of this; lanthanides bind to a number of sites on antibodies, including one on Fc.

Lerner: It is not going to be difficult to build good coordination sites. What is going to be hard is approximating the metal to the substrate.

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Abstract: We describe a technology for generating recombinant polyclonal antibody libraries (PCALs) that enables the creation and perpetuation of standardized mixtures of polyclonal whole antibodies specific for a multiantigen (or polyanitigen). Therefore, this technology combines the advantages of targeting multiple antigenic determinants -- high avidity, low likelihood of antigen 'escape variants', and efficient mediation of effector functions, with the advantages of using monoclonal antibodies -- unlimited supply of standardized reagents and the availability of the genetic material for desired manipulations. The technology for generating recombinant polyclonal antibody libraries begins with the creation of phage display Fab (antibody) libraries. This is followed by selection of sublibraries with desired antigen specificities, and mass transfer of the variable region gene pairs of the selected sublibraries to a mammalian expression vector for generation of libraries of polyclonal whole antibodies. We review here our experiments for selection of phage display antibody libraries against microbes and tumor cells, as well as the recent literature on the selection of phage display antibody libraries to multiantigen targets.

INTRODUCTION

The antibody response of vertebrates to most antigens is polyclonal and targets multiple epitopes on the antigen surface [1,2]. This characteristic has co-evolved with the effector mechanisms mediated by the Fc regions of antibodies -- such as complement binding with production of C3b, opsonization/phagocytosis, and antibody-dependent cellular cytotoxicity (ADCC) -- that serve to eliminate the antigen [1-4]. Thus, triggering of effector functions requires a high density of antibodies on the antigen surface for sufficient cross-linking of Fc receptors on effector cells and for efficient C1q binding [5-7]. When the immunogen is a living cell, such as a microbe or a tumor cell, the polyclonality of the antibody response helps guard against the development of cell 'escape variants' that are no longer recognized by the antibodies. This is because the chance that a given cell will simultaneously lose all the target epitopes is (in most cases) essentially zero.

Passive immunotherapy with serum-derived polyclonal antibodies has been used for many years. The use of polyclonal human immunoglobulin (human gamma globulin) -- for the

treatment of patients with agammaglobulinemia, immunocompromised patients, and patients with severe microbial infections -- is generally effective and shows no adverse reactions [8-13]. Treatment of mice with serum-derived murine polyclonal antibodies has been shown to prevent development of a murine tumor [14]. Furthermore, occasional successful treatment of human malignancies, such as melanoma and renal cell carcinoma, with polyclonal antibodies derived from animals or from humans has been reported [15,16].

Despite their efficacy in many applications, the use of conventional polyclonal antibodies is limited by: short supply of serum antibody from immunized animals or from humans; inability to modify the antibodies because the genes are not available; and, in cases where a human cell population (malignant or normal) is targeted, the likely loss of the vast majority of the antibody population if negative selection were performed to eliminate major cross-reactivities with other tissues or cell populations. This is because many cell surface antigens are expressed on many different cell types.

Unlike polyclonal antibodies, monoclonal antibodies provide an unlimited supply of standardized reagents [17-19], and their heavy (H) and light (L) chain genes can be readily cloned and manipulated. However, monoclonal antibodies target single epitopes. Therefore, they are much less efficient at activating effector mechanisms than

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few phage particles can be amplified indefinitely if they are used to infect the bacterial host. This powerful system has been used by other investigators to select and clone-out phage encoding monoclonal antibody fragments to happens, proteins, viruses, and cancer cells [33-42] as an alternative to the hybridoma technology.

In contrast, our laboratory has adapted the Fab phage display system to generate polyclonal antibodies (PCALs, pronounced "P"- "Cals") [43-47]. Instead of isolating monoclonal Fab phage particles, the Fab phage display libraries are maintained as polyclonal mixtures and subjected to positive and negative selection; positive selection to recover those phage particles with desired antigen specificities, and negative selection to remove those phage particles with undesired specificities (for example those with certain cross-reactivities). After amplification of the selected sublibraries, the selected antibody genes are transferred, in mass, from the phage vector population to a mammalian vector that provides complete constant region genes and appropriate transcription regulatory elements for expression of whole, glycosylated IgG antibodies in mammalian cells. Thus, the library that was selected at the Fab phage display level can be expressed -- after transfection of the mammalian vector population into mammalian cells -- as a library of polyclonal whole antibodies that can mediate effector functions. Because the transfected cells are immortal, the cell population producing the IgG polyclonal library can be perpetuated indefinitely, just like hybridoma cells. Alternatively, this cell population can be recreated as desired by transfection of the mammalian vector population into mammalian cells [Fig. (1)].

Polyclonal antibody libraries can be manipulated to eliminate undesirable specificities and have the unique advantage (not shared by conventional polyclonal antibodies) that desired specificities can be amplified. Thus, even if 99.99% of the antibody population to cancer cells is lost by absorption with normal cells, a library of 10^8 members will be reduced to 10^4 members, which could be amplified to generate unlimited supplies of the (still large) sublibrary. By comparison, a conventional polyclonal antibody preparation will be essentially lost after absorption to remove major reactivities against normal human cells.

PCALs (obtained by mass antigen-selection and mass transfer of selected variable region gene pairs without isolating or characterizing individual library members) differ from collections of monoclonal antibodies (each of which had been selected for

polyclonal antibodies (hence the need for toxic tags in therapeutic applications [20-23]. Furthermore, the likelihood of cell 'escape variants' -- that are no longer recognized by the antibody -- is much higher for monoclonal than polyclonal antibodies.

To combine the advantages of polyclonal and monoclonal antibodies, we have developed a technology for generating polyclonal antibody libraries. This technology enables the perpetuation of standardized mixtures of polyclonal antibodies specific for an antigen or a multiantigen target (a polyanitigen). Hence, it combines the advantages of targeting multiple antigenic determinants (high avidity, low likelihood of antigen 'escape variants', and efficient mediation of effector functions) with the advantages of using monoclonal antibodies (unlimited supply of standardized reagents, and the availability of the genetic material for desired manipulations such as the replacement of mouse constant regions by human constant regions to generate chimeric antibodies [24,25].

The generation of polyclonal antibody libraries with desired specificities is made possible by the technology for displaying Fab antibody fragments on the surface of phage particles to generate so called "Fab phage display libraries" [26-29]. In this system the genetic material encoding Fab fragments is obtained from the B lymphocytes of immunized animals (or from humans) and cloned into a phagemid vector such that the genetic material encoding the Fab is attached to the genetic material encoding a phage coat protein. (Fab is comprised of 2 chains: the L chain and the Fd chain. The L chain contains the variable [V] and constant [C] region [VL-CL]; and the Fd chain contains the V region and the first H chain constant domain [VH-CH1].) On transformation of bacteria with these phagemid vectors (and superinfection with helper phage), phage particles that display Fab on their surface are generated because the Fab is embedded in the phage coat via the coat protein to which it is attached. Because each phage particle contains a different vector molecule for its genome, each phage particle displays a different Fab on its surface. Phage libraries larger than 10^8 different members can be generated. The libraries can be selected for binding to specific antigens (positive selection) by affinity chromatography [30-32], including panning on antigen-coated surfaces [29].

The beauty and power of the phage display system is the coupling of a selectable function (binding to an antigen) to the genetic material that encodes that function. This is because the selected phage have a replication function and therefore a

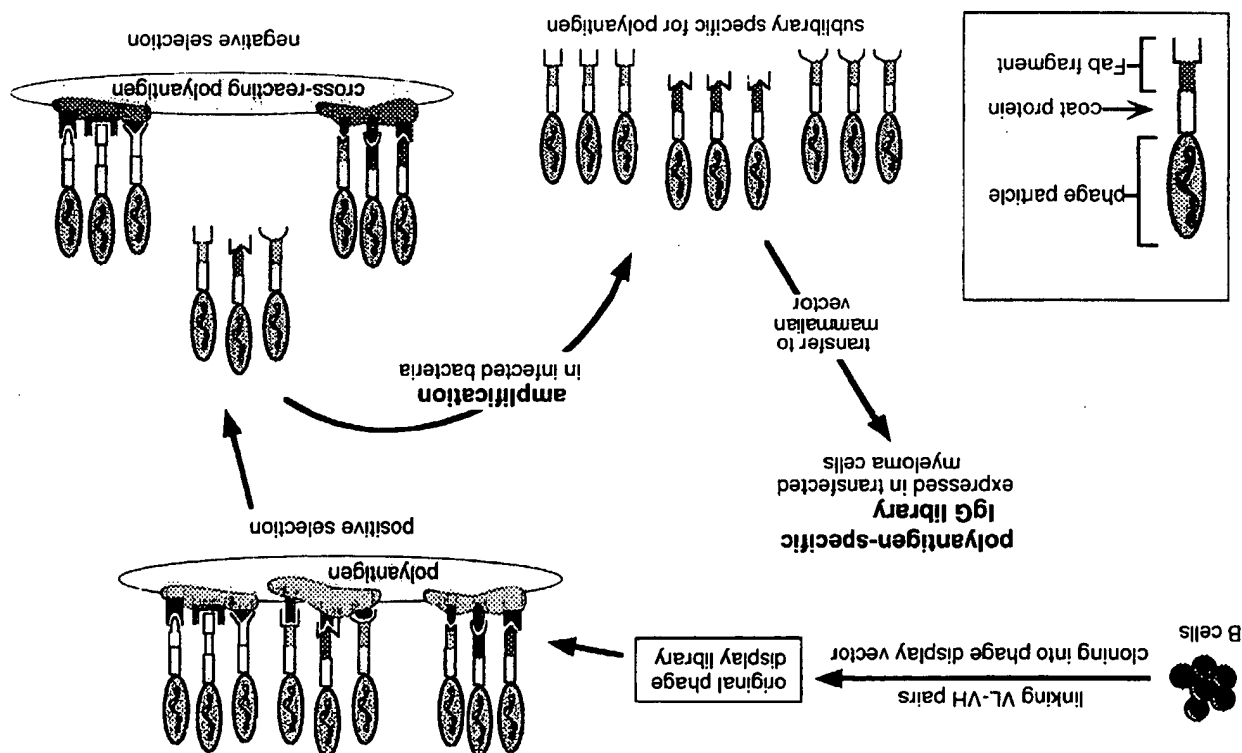


Fig. (1). Scheme for production and selection of a polyanitgen-specific polyclonal antibody library.

antigen, with a high signal-to-noise ratio. This concept is exemplified schematically in Fig. (2).

THE SYSTEM FOR GENERATION OF PCALS

We have developed a system of phagemid and mammalian bidirectional vectors that facilitates the mass transfer of linked VL-VH region gene pairs [43,44], from antigen-selected sublibraries, without loss of the VL-VH combinations. The key feature of the transfer is that the VL and VH region genes are linked head-to-head ($\rightarrow\rightarrow$) in opposite transcriptional orientations. Linking of VL and VH region genes is done by reverse transcription - polymerase chain reaction (RT-PCR).

Primers, cDNA Synthesis, and VL-VH cDNA Linking

A method for cDNA synthesis and VL-VH cDNA linking was developed, and appropriate V and C region primers were designed [44,45]. In this method, RNA is obtained from B cell and plasma cell-containing tissues of immunized mice and used to prepare combinatorial libraries of VL-VH region gene pairs, linked head-to-head ($\rightarrow\rightarrow$)

antigen specificity). This is because PCALs contain individual antibodies which may or may not be specific for the target, but the collection of the individual antibodies recognizes the target antigen way above the background of any cross-reacting

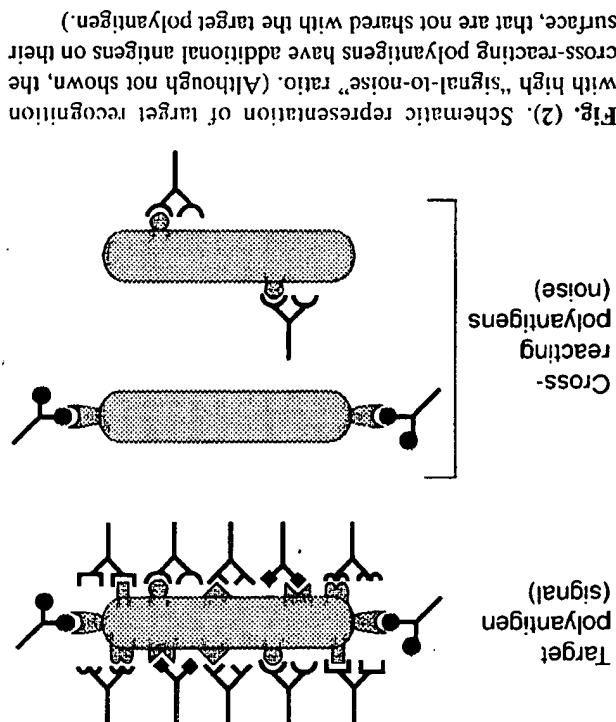


Fig. (2). Schematic representation of target recognition with high "signal-to-noise" ratio. (Although not shown, the cross-reacting polyanitgens have additional antigens on their surface, that are not shared with the target polyanitgen.)

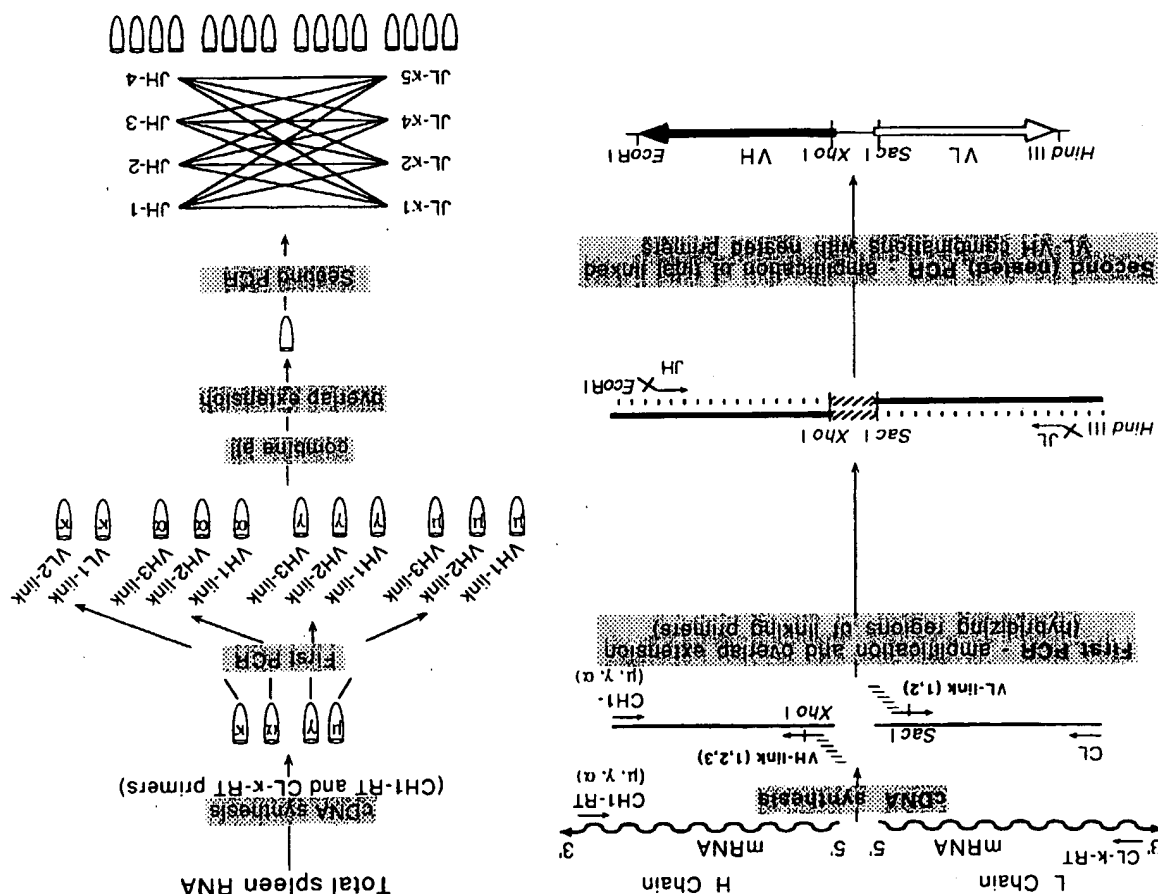


Fig. (3). General scheme for linking and amplifying VL-VH region gene pairs in opposite transcriptional orientations. VL-VH products are obtained after cDNA synthesis and consecutive PCR steps. See Fig. (4) for primer sequences.

involve PCR using nested primers at high stringency to ensure that only Ig sequences are amplified [45].

The PCR-amplified L and H chain sequences are combined into a single tube, to allow hybridization of the complementary VL and VH tails and overlap extension to generate head-to-head-linked VL-VH region gene pairs. The product of the overlap extension reaction is then used in an array of 16 separate PCRs, each amplified with a different pair of JL and JH primers that hybridize to the four Jk and four JH mouse genes and which contain a *Hind* III or *Eco*R I site for the JL and JH primers, respectively [see Fig. (3) for scheme and Fig. (4) for primer sequences].

Generation of Fab Phage Display Libraries in a Bidirectional Phagemid Vector

A bidirectional phagemid vector was generated by modification of the unidirectional Fab phage

conditions (37°C). However, subsequent steps First PCR is done under very low stringency, the templates) in this minimal set of V primers, the large number of mismatches (to prospective (4) for primer sequences). Because of the relatively complementary to the tail of VH primers [see Fig. leader sequences. The tail of VL primers is necessary for subsequent insertion of promoter and for the 2 VL and 3 VH primers, respectively) includes a restriction enzyme site (*Sac*I and *Xho*I primer provides a tail (link) for VL-VH linking that 5' end of VL or VH region genes. Each VH or VL primers and a forward primer that hybridizes to the chain) PCRs using μ , γ , α , or κ nested reverse the four tubes is then used in 3 (H chain) or 2 (L chains. The first strand cDNA library from each of all four mouse γ isotypes), to α H chains, or to κ L primer hybridizing to μ H chains, to γ H chains (of different tubes, each containing a different reverse synthesis of VL and VH region genes is done in 4 gene pairs is shown in Fig. (3). First strand cDNA scheme for RT-PCR and linking of VL-VH region in opposite transcriptional orientations. The general

phagemid vector pComb3 [29], by a series of modifications [44,47]. The cassette contains the *lacZ* and *lac* promoters to drive expression of the κ and λ chains respectively. Although the leader sequences for both chains have the *pelB* leader amino acid sequence, the nucleotide sequences differ at many positions [44], and therefore, deletions are unlikely to occur during replication of the vector. The bacterial promoter-leader cassette also includes the selectable marker ZeocinTM [49,50] (driven by the synthetic promoter EM-7), which ensures that only vector molecules that have incorporated the cassette are perpetuated during library construction [47].

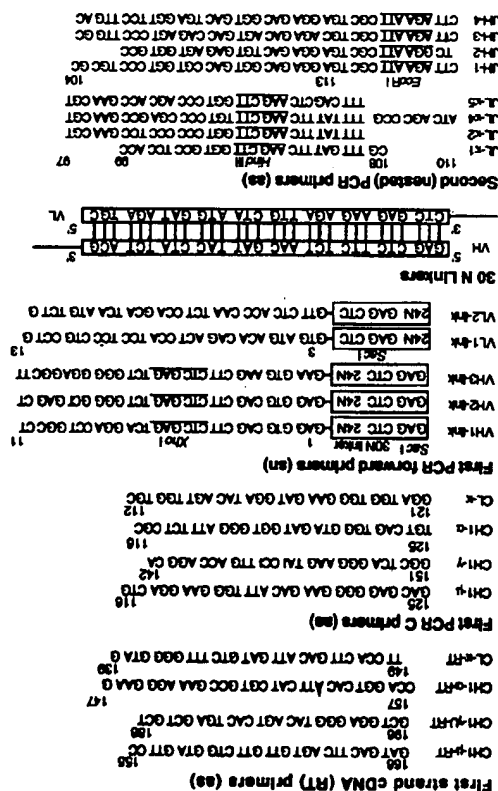
Transformation to produce colonies and infection of bacteria to produce phage display libraries are done as described [29]. The Fab phage display libraries can be selected for binding to polyanthens, to generate specific sublibraries (described in subsequent sections).

Mass Transfer of VL-VH Region Gene Pairs from the Phagemid Vector to a Bidirectional Mammalian Expression Vector

Generation of polyclonal whole antibodies requires the mass transfer of selected VL-VH region gene pairs from the phagemid vector to a mammalian expression vector, without loss of the bidirectional expression vector. Therefore, a bidirectional mammalian vector for expression of mouse IgG2b antibodies was constructed ([43] and C.-Y. Kao and J. Sharon, manuscript in preparation). This vector, denoted #577 PMDV-IgG2b [Fig. (6), right side] contains the mouse γ 2b heavy chain C gene and the mouse κ light chain C gene in opposite transcriptional orientations, as well as the *gpt* selectable marker, and mammalian transcription termination and polyadenylation sites.

VL-VH region gene pairs linked head to head ($\rightarrow\rightarrow$) in opposite transcriptional orientations, are transferred, in mass, between the (circular) bidirectional phage display vector and the (circular) mammalian expression vector. The transfer from a phage display to a mammalian expression vector requires opening the phage display vector with *Sac* I and *Xho* I [Fig. (6a)] between the VL and VH amino termini and replacing the prokaryotic *lPZeoP* cassette with a mammalian *lPEHP*m cassette (which contains Ig promoter and leader sequences in opposite orientations as well as a heavy chain enhancer), yielding the intermediate vector shown in Fig. (6b). The VL-VH pairs including

Fig. (4). Oligonucleotide primers used for library construction. The antisense and sense strands are denoted by "as" and "sn", respectively. Restriction sites are underlined. Corresponding amino acid numbers in the Kabat system [77] are shown above the sequences. Linker regions (the 30 nucleotide tails plus the first nucleotide of the VL or VH region) are indicated. N, nucleotide(s).



display vector pComb3 [29]. The bidirectional vector [48 ph3mu- γ 1, Fig. (5a)] contains, in opposite transcriptional orientations, a mouse κ gene and a mouse γ 1 CH1 gene segment attached to DNA encoding the carboxyl terminal end of the phage coat protein cpIII [44]. VL-VH region gene pairs linked head-to-head, in opposite transcriptional orientations, are cloned between the *Hind* III and *Eco* R I sites of the ph3mu- γ 1 vector [Fig. (5a)] to generate a library of vectors [ph3VL-VH- γ 1b, see Fig. (5b)]. Because the VL and VH region genes, in each pair, are separated by *Sac* I and *Xho* I restriction enzyme sites, a cassette containing head-to-head bacterial promoter (P) and leader (l) sequences is obtained from vector #560 *pPZeoP* [Fig. (5b)] and cloned between the *Sac* I and *Xho* I sites of ph3VL-VH- γ 1b to drive expression of κ chain and λ chain of Fab cpIII proteins. This generates a library of Fab phage display vectors [ph3-VL-*pPZeoP*-VH- γ 1b, Fig. (5c)]. The bacterial promoter-leader cassette in vector #560 *pPZeoP* had been generated from

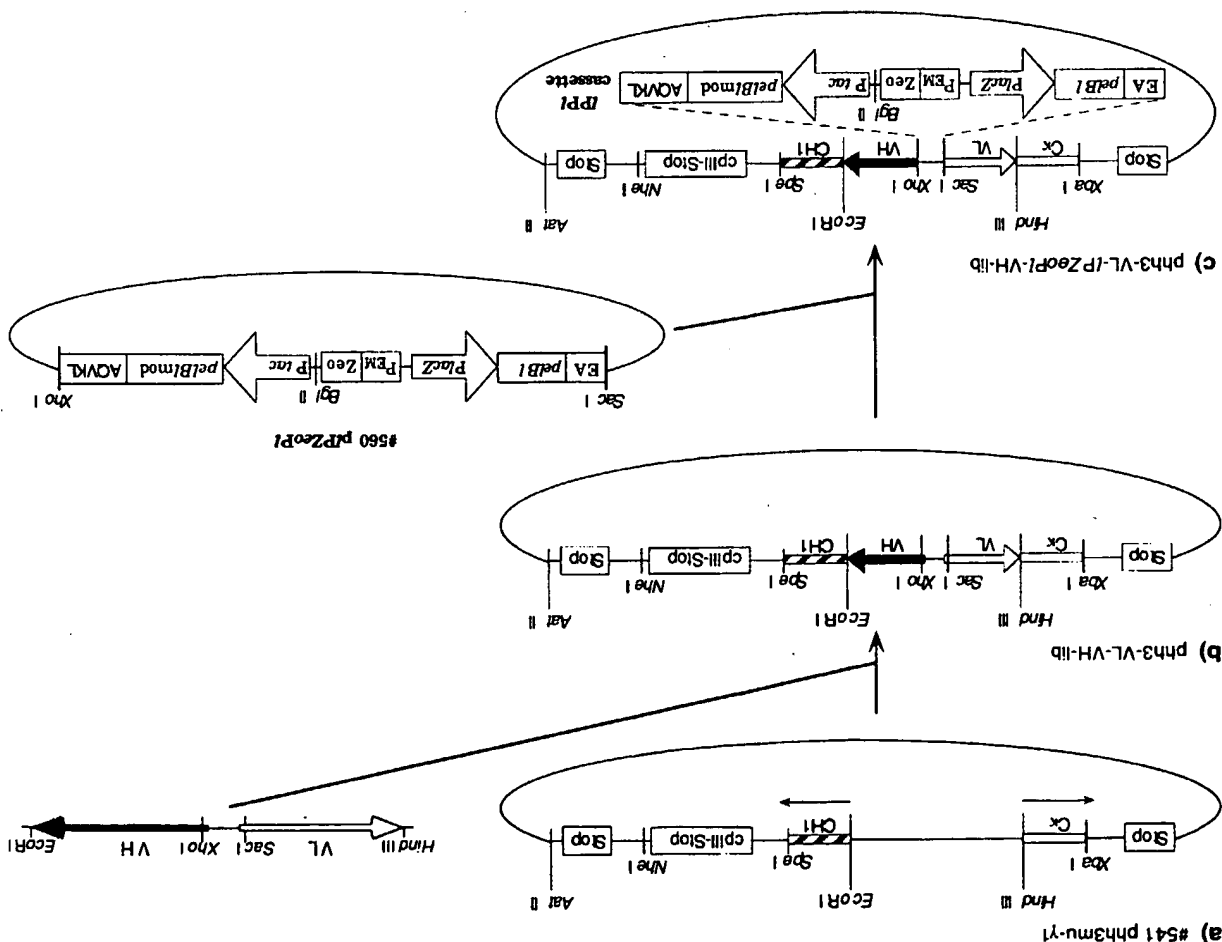


Fig. (5). Scheme for construction of Fab phage display libraries (partial maps and not to scale); all vectors are circular. The direction of transcription is indicated by arrows and by arrow heads on promoters and variable region genes.

Symbols: P, promoter; l, leader sequence; lmod, leader sequence with modified nucleotide sequence; Stop, translation termination; Zeo, gene for Zeocin™ selectable marker. Amino acids encoded by the vectors are shown in one letter code.

TESTING OF THE SYSTEM FOR GENERATING POLYCLONAL ANTIBODY LIBRARIES

The functionality of the bidirectional phage display and mammalian expression vectors as well as the generation and transfer of linked VL-VH

region gene pairs were tested [43,44]. In one series of experiments [44], V region gene pairs derived from an A/J mouse that had been immunized with the hapten *p*-azophenylarsenate (Ars) coupled to keyhole limpet hemocyanin (KLH) were selected for Ars-binding in the phage display vector, transferred to the mammalian vector, and expressed as a mouse IgG2b PCAL. As expected, individual IgG2b antibodies from the PCAL had V region sequences and Ars-binding characteristics similar to those of anti-Ars hybridomas [44].

GENERATION OF POLYCLONAL FAB PHAGE DISPLAY LIBRARIES TO POLYANTIGENS

Using our system for PCAL generation, described above, we have generated Fab phage

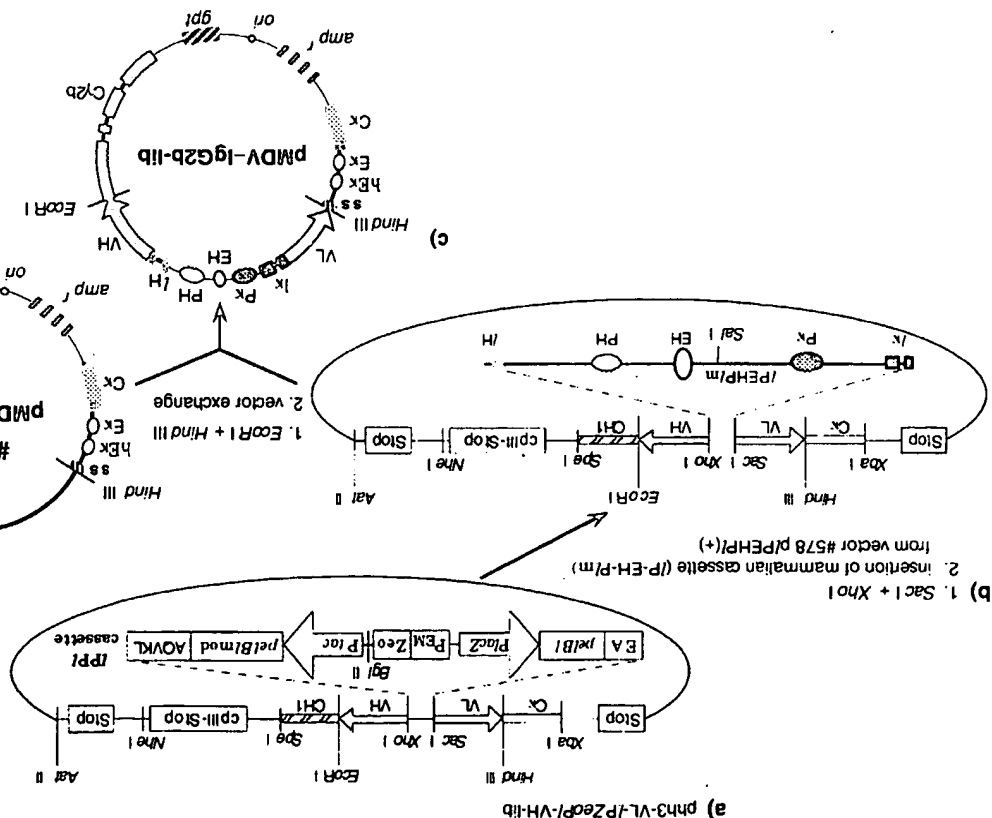


Fig. (6). Transfer of V region gene pairs between bidirectional phage display and mammalian expression vectors (partial maps and not to scale).

Symbols: Prokaryotic elements are as in Fig. (5). Mammalian regulatory elements are oval shaped. amp^r, ampicillin resistance; ori, prokaryotic origin of DNA replication; P, promoter; E, enhancer; L, leader sequence; ss, splice site; hum, human (all other mammalian regulatory elements are murine).

display libraries to infectious agents and cancer cells.

Generation of a Polyclonal Fab Phage Display Library to the Protozoan Parasite *Cryptosporidium parvum*

Cryptosporidium parvum is a protozoan parasite that causes severe disease in AIDS patients, for which there is no effective treatment [46]. A Fab phage display library was constructed from the RNA of spleen, intestine, nasopharynx, and bone marrow of *C. parvum*-immunized BALB/c mice. The Fab-displaying phage library was selected for binding to an oocyst/sporozoite preparation of *C. parvum*, generating an anti-*C. parvum* Fab phage display library of 5.2×10^4 members, which was tested for antigen-binding by direct ELISA. As shown in Fig. (7), the *C. parvum*-selected phage library bound to a *C. parvum*-coated plate whereas the unselected library and a negative control of

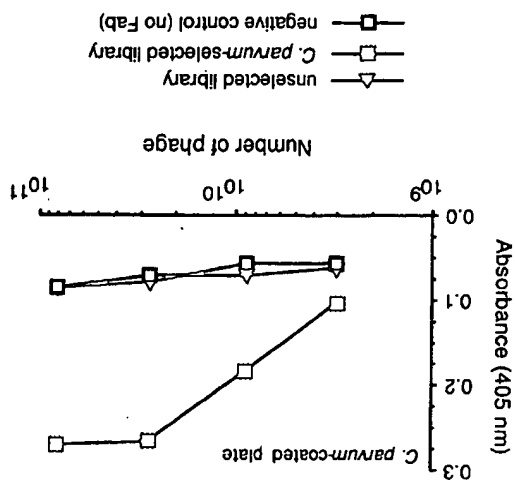


Fig. (7). Specificity of anti-*C. parvum* Fab phage display library shown by direct ELISA.

Generation of Fab Phage Display Libraries to Human Ovarian Tumor Cell Membranes and Sheep Red Blood Cells

Cells from a surgically-resected human ovarian carcinoma (designated OC2), and sheep red blood cells (SRBCs) as control, were separately used to immunize mice [45]. BALB/c mice were immunized with either OC2 membranes or SRBCs by 3 intraperitoneal injections in complete Freund's adjuvant. RNA samples obtained from the spleens of the immunized mice were separately used to prepare Fab phage display libraries, using the system and primers described above. Each library was subjected to two consecutive panning on wells coated with the immunizing polyanigen (OC2 or SRBC membranes, each library in two wells of a 24-well plate). Direct binding solid phase ELISA of the anti-OC2 and anti-SRBC Fab phage display libraries showed that successive panning increased specificity for the panning membranes [45]. Furthermore, binding of the second OC2 panned library to an OC2 membrane-coated plate was specifically inhibited by OC2 membranes but not by SRBC membranes. Conversely, binding of the second SRBC panned library to an SRBC membrane-coated plate was specifically inhibited by SRBC membranes but not by OC2 membranes [45].

Generation of a Fab Phage Display Library to the Human Breast Cancer Cell Line BT-20

A polyclonal Fab phage display library to BT-20 cells was constructed from RNA of spleen, bone marrow, and intestine from a BALB/c mouse that had been immunized with BT-20 cells [47]. To select an Fab phage sublibrary that reacts with the BT-20 carcinoma cells, phage were subjected to two consecutive rounds of panning on fixed BT-20 cells. The first pan yielded a library of 8×10^4 members, whereas the second pan yielded a library of 3×10^6 members. Analysis of the unpanned and panned Fab phage libraries by ELISA on fixed BT-20 cells showed that the second pan library binds better than the first pan library which, in turn, binds better than the unpanned library [47].

To confirm the specificity of the second pan Fab phage library for BT-20 cells, the library was tested in a criss-cross inhibition ELISA in conjunction with the panned anti-SRBC Fab phage library. BT-20 membranes inhibited the binding of the anti-BT-20 phage library to solid phase BT-20 cells in a

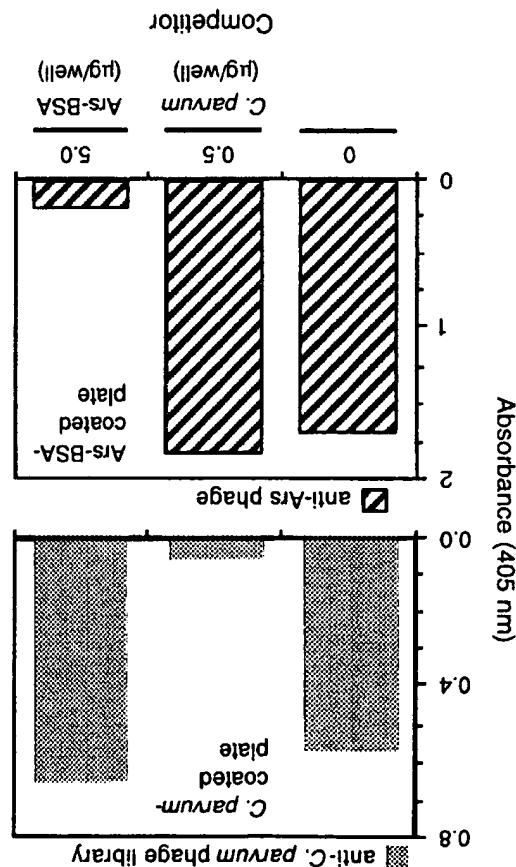


Fig. (8). Specificity of anti-*C. parvum* Fab phage display library shown by inhibition ELISA.

The specificity of the *C. parvum*-selected phage library was further demonstrated by a criss-cross inhibition ELISA using both the anti-*C. parvum*-selected phage and phage displaying Fab specific for the Ars hapten. As seen in the top panel of Fig. (8), the binding of the anti-*C. parvum* phage to solid phase *C. parvum* was inhibited by preincubation with the oocyst/sporozoite preparation with Ars coupled to bovine serum albumin (BSA). Conversely, binding of the anti-Ars phage to solid phase Ars-BSA was inhibited by preincubation with Ars-BSA but not by preincubation with the oocyst/sporozoite preparation of *C. parvum* [see bottom panel of Fig. (8)].

Restriction fragment length polymorphism (RFLP) analysis and nucleotide sequencing of several members of the *C. parvum*-selected library indicated that the selected library is diverse.

dose-dependent manner but not of the anti-SRBC phage library to solid phase SRBC membranes. Conversely, SRBC membranes inhibited the binding of the anti-SRBC phage library to solid phase SRBC membranes in a dose-dependent manner but not of the anti-BT-20 phage library to solid phase BT-20 cells [47].

RECENT LITERATURE ON SELECTION OF PHAGE DISPLAY ANTIBODY LIBRARIES TO MULTANTIGEN TARGETS

Selection of phage displaying antibody fragments with desired antigen specificity, from a phage display antibody library with no demonstrable specific binding to the desired antigen(s), can be achieved by any method that separates antigen-binding phage from non-antigen binding phage. Commonly, antigen is immobilized on a solid surface and phage incubated with the antigen to capture binding phage, a method known as panning [29,33,51,52]. The solid surface is washed to remove non-binding phage, the binding phage are eluted and used to infect bacteria, resulting in amplification of the antigen-selected phage. Elution of bound phage can be achieved by any of several methods: using acidic solutions such as HCl-glycine [51], with basic solutions like triethylamine [33], by competition with antibodies to the antigen [53], or by enzymatic cleavage of a protease site engineered between the antibody fragment and the gpIII protein [54]. Alternatively, direct bacterial infection without chemical elution of phage has been used [55]. Sequential rounds of selection are often performed to obtain a high percentage of antigen-specific phage [29,33,51-53,55-65].

For selection of antibody-displaying phage (often referred to as "phage antibodies") to a multiantigen target (i.e. polyanitigen), such as microbial or mammalian cells, panning as well as other methods have been used. Several groups have reported the successful isolation of phage antibodies binding to microbes by selecting on whole microbes [46,56,57,66]. Monolayers of adherent cancer cells and cell lines transfected to express an antigen of interest, either fixed [47,58-60] or non-fixed [39,61,62], have been used to successfully isolate specific phage antibodies. Many groups have also used such cell lines in suspension to select for binding phage [42,63-65,67-71]. The methods in which the phage antibodies that bind to the target cells are separated from the non-binders are diverse: centrifugation to

pellet bound phage and target cells leaving non-binding phage in the supernatant [42,63-65], flow cytometry to isolate a specific cell population with bound phage [67,69,70], and magnetic beads to sort desired cell-binding phage [68,71]. Isolation of phage antibodies to cell surface antigens has also been reported by groups using cancer tissue sections on slides [72] and thymic tissue fragments [73].

These methods of selection are used to isolate binding phage (positive selection), however, one may wish to rid the library of phage antibodies that may cross-react with or have epitopes in common with another polyanitigen (e.g. normal, non-cancerous cells). To achieve this one or more rounds of negative selection may be performed before or after positive selection, using normal cells (or any other polyanitigen of choice) to absorb the unwanted cross-reactive phage antibodies [39,62,64]. A round of negative selection may be performed simultaneously with the positive selection by combining both positively selecting target cells (e.g. cancer cells) and negatively selecting absorber cells with the phage library, then separating the desired selecting target cells with binding phage from the absorber cells with binding phage [67,68]. Separation may be achieved with flow cytometry [67], magnetic beads [68], or any method to sort the target cells from the absorber cells. Once separated, only the phage bound to the target cells would be eluted.

There are many selection strategies one could use in the creation of polyclonal antibody libraries to polyanitigens, as outlined above, but the strategy must be carefully designed because the composition of the output library of phage antibodies will depend on the method used. For example, one group's initial attempts to pan on confluent monolayers of transfected CHO cells yielded predominantly phage antibodies that were reactive with serum proteins. It was hypothesized that the serum proteins present in the cell culture medium adhered to the flask during cell growth and therefore were present during phage selection. The problem was overcome by a strategy that kept cells in suspension during selection [63].

In the same study it was also noted that as the number of selection rounds increased, the diversity of selected phage antibodies decreased, with certain clones dominating in later selection rounds [63]. The same problem was discussed at a recent antibody engineering conference, and it was pointed out that during selection procedures competition may cause loss of many potential

L chain	=	Light chain
PCAL	=	Polyclonal antibody library
PCR	=	Polymerase chain reaction
RT	=	Reverse transcription
SRBC	=	Sheep red blood cell
VH	=	Heavy chain variable region
VL	=	Light chain variable region

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CONCLUSION

binders, resulting in output phage dominated by a few clones. This problem becomes even worse when using complex antigens such as whole cells. The presenting group solved the problem by doing only one round of selection [74]. Thus, for selection of polyclonal phage antibodies to polyanitigens, it is especially important that the number of selection rounds be limited to one or two, as more selection rounds may restrict the size of the selected library.

The technology is now available for the production of polyclonal antibody libraries that will simultaneously recognize many epitopes on a multitude of antigens on tumor cells, microbes, or any other polyanitigens, greatly reducing the chance of escape variants. These standardized antibody mixtures will be available in unlimited supply, will be amenable to alteration by genetic manipulations, and will be efficient at mediating effector functions to eliminate target polyanitigens.

Regarding future FDA approval, PCALs should fall under the same category as such clinically used polyclonal antibody products as human gamma globulin preparations, anti-thymocyte globulin (ALG) and anti-thymocyte sera (ATS) [75,76]. Like these products, every PCAL batch will have to be tested for safety, but PCALs are expected to show much less batch-to-batch variability.

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ABBREVIATIONS

Ars	=	p-Azophenyldarsonate
BSA	=	Bovine serum albumin
C region or domain	=	Constant region or domain
H chain	=	Heavy chain

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Universal Antibody Libraries on Phage and Bacteria

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Combinatorial IgM Libraries

It is estimated that about 10^6 - 10^8 antibodies with different binding properties are present in the immune system at any one time. This number is sufficient to bind most antigens including synthetic compounds such as dinitrophenol that the immune system has never encountered. If it were thus possible to create antibody libraries with comparable numbers of truly diverse antibodies then it should be feasible to select an antibody from this library against any particular antigen.

A highly diverse antibody library can be obtained by amplifying and randomly combining chains of the naive IgM repertoire. These antibodies are expressed mainly on the surface of unactivated B lymphocytes. Attachment of antigen and interaction with T-helper cells then activates the B cell, which eventually matures into an IgG-secreting plasma cell. This process is accompanied by a somatic hypermutation of the antibody to increase its affinity for the antigen. In contrast to the employment of individual primers for each of the variable chain families [1, 2] we devised a strategy of minimal priming to generate a naive IgM library of more than 10^7 individual clones [3]. RNA from the peripheral blood lymphocytes of 20 donors was pooled prior to cDNA synthesis to reduce the relative amount of specific RNAs from any abundant B cell clones of individual donors. An average of 5×10^6 cells with a viability of $>95\%$ were prepared from each donor. The quality of the RNA was controlled by Northern blotting using a radioactively labelled oligonucleotide that hybridizes to the C-terminus of the constant region of human κ chains. The size of the generated cDNAs ranged up to 5 kb. About $1 \mu\text{g}$ of cDNA was used per polymerase chain reaction (PCR) amplification.

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Given an average length of 1 kb, this amount contains 10^{12} cDNA molecules. Assuming that at least 1 mRNA out of 1,000 encodes for antibody chains in B cells (which represent > 10% of the lymphocyte preparation), then at least 10^8 molecules of antibody cDNA were present in the starting material for each PCR. This corresponds to the number of different B cells used for the preparation. It is highly probable, therefore, that the complexity of the library is maintained during the preparation of antibody DNA.

We used backward primers homologous to the N-terminal part of the constant region instead of backward primers to the framework 4 region of the variable chain, as described by Marks et al. [1, 2] to reduce the effect of different primer affinities for each family of antibody DNA. Since the backward primers in our system are derived from highly conserved constant chain sequences, only the forward primers bear a risk of not priming a particular antibody DNA. In addition, the PCR conditions were optimized for the lowest possible hybridization temperature to enable priming from sequences with many mismatches. A meaningful statistical analysis of the variability is not possible, but partial sequencing of 19 individual clones of the κ sublibrary showed that 18 encode antibody DNA, and all these chains were different. The small proportion of nonantibody genes would appear to be quite acceptable as a consequence of achieving maximum variability.

The antibodies in this 'naive' library were expressed as single peptide chains after randomly combining the antigen-binding variable domains of κ or λ and μ chains. The peptide linker between the heavy and light chains consisted of approximately 18 amino acids containing an epitope recognized by the antitubulin monoclonal antibody YOL/34. This enabled the antibodies to be easily identified on Western blots. For optimal production of the antibodies the antibody DNA was cloned into the antibody expression vector POPE 90 [4].

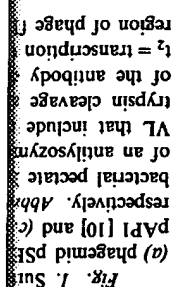
It was often found that a significant percentage of the clones from antibody libraries that had been amplified by PCR from peripheral blood lymphocytes produced antibodies that were not in the expected size range. To reduce the number of these deletion mutants, we constructed the antibody expression vector pLAB in which DNA coding for a single-chain antibody was inserted into the gene encoding β -lactamase at the 3'-terminus of its signal sequence [5]. After transforming *Escherichia coli* with this vector, a fusion protein with a functional β -lactamase domain was produced that was able to protect the bacteria from the action of ampicillin. Libraries containing deletion mutants can therefore be usefully propagated with this vector, since only those inserts that are in frame with β -lactamase will survive.

At least five of the six hypervariable regions appear to consist of only a small repertoire of main chain conformations [7]. The CDR3 region of the heavy chain hypervariable regions, however, could not be classified into distinct known canonical structures. This is not surprising since the H3CDR region is the most variable. It also appears to make the largest contribution to the surface area available for contact with the antigen [8]. Substitution of the H3CDR region of a tetanus toxoid-binding Fab fragment with random sequences to create a semisynthetic library has demonstrated the potential of synthetic libraries for isolating novel specificities [9]. The randomization of the remaining five hypervariable regions, however, could conceivably create more problems than gains in the generation of highly diverse antibody libraries. If, for example, only particular sequence combinations can be accommodated in a restricted repertoire of canonical structures, then the chances of synthesizing an antibody with acceptable sequences in all six hypervariable regions are extremely low. On the other hand, these structures may just be reflecting the structural restraints imposed by the framework sequences and the more limited sequence variability in these regions than in H3CDR. It will therefore probably be necessary to systematically compare the quality of several synthetic libraries of antibodies containing an increasing number of restrictions in the randomness of each hypervariable region in order to choose conditions for obtaining the most diversity.

For screening the highly diverse libraries mentioned above, that might contain at least 10^9 different antibodies, a method of clonal selection is required similar to that of the immune system in which the antibody is physically connected to its own gene [10]. This can be achieved by expressing the antibody on the surface of bacteria or bacteriophage. An excellent means

For screening the highly diverse libraries mentioned above, that might contain at least 10^9 different antibodies, a method of clonal selection is required similar to that of the immune system in which the antibody is physically connected to its own gene [10]. This can be achieved by expressing the antibody on the surface of bacteria or bacteriophage. An excellent means

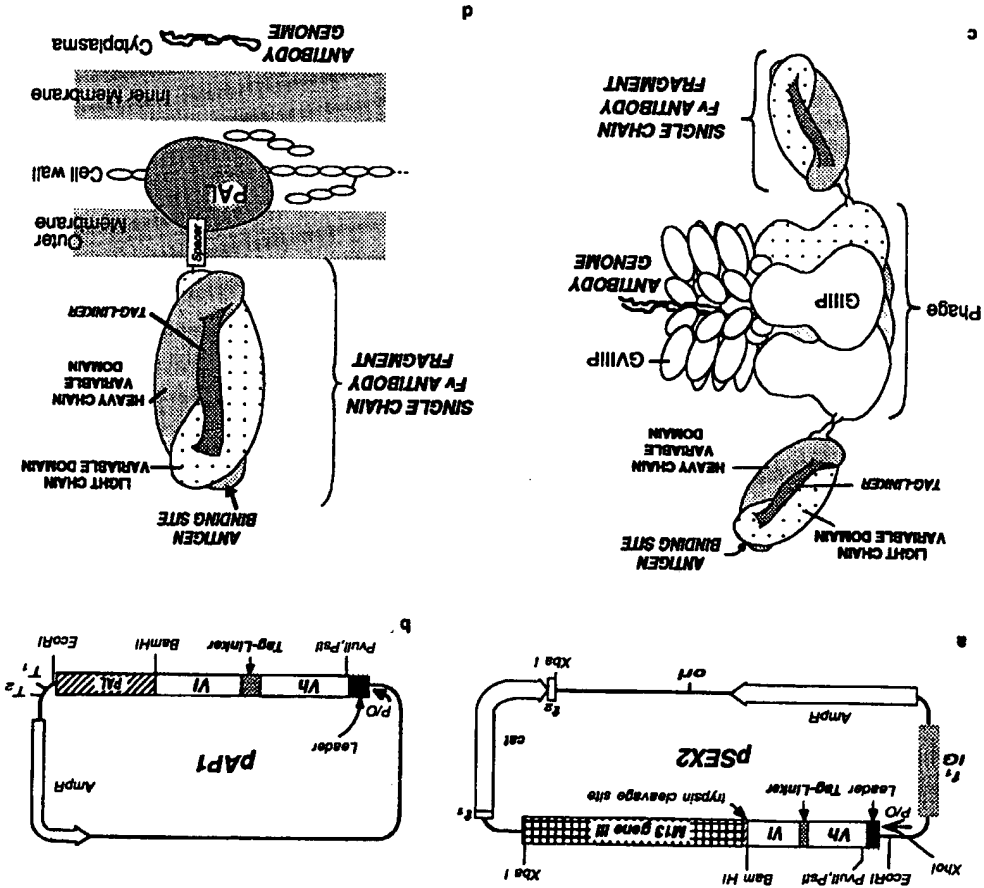
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Fig. 1. Surface expression vectors for the display and screening of antibodies: (a) phagemid pSEX2 [14]; (b) antibody-peptidoglycan-associated protein expression plasmid pAP1 [10] and (c, d) artist's impression of antibody display obtained with pSEX2 and pAP1, respectively. Abbreviations: P/O = promoter/operator; Leader = signal peptide sequence of an antibody; Tag-Linker = oligo encoding 18 amino acids linking VH and VL that include an α -tubulin epitope recognized by the monoclonal antibody YOL1/34; trypsin cleavage site = LysAspIleArg. This optional sequence permits proteolytic cleavage of the antibody domains from pIII; cat = chloramphenicol acetyltransferase gene; t_1 and t_2 = transcription terminators; ori = origin of DNA replication for ColEI; Π IG = intergenic region of phage II.



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J Mol Biol 1991;222:581-597.

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of this system for screening antibody libraries is presently being investigated. antibodies were accessible at the surface of intact bacteria. The applicability 1b, d). Immunofluorescence studies on unfixed cells showed that functional N-terminus of the so-called peptidoglycan-associated lipoprotein [17] (fig. to the surface of *E. coli*, we have fused a single chain Fv fragment to the particularly useful in the search for catalytic antibodies. To target antibodies could be used for selection. The latter procedure could prove to be Alternatively, magnetic beads or highly sensitive colony-screening assays single cells expressing antibodies using a fluorescence-assisted cell sorter. libraries. Using fluorescent tags, for example, it should be possible to isolate of proteins and may provide an alternative means of screening antibody Bacterial surfaces would be more suitable for presenting high numbers. the heavy and light chains, and by antisera to their N-terminal sequences. monoclonal antibody to the tubulin epitope in the linker sequence between thus greatly facilitating its analysis. The fusion protein was identified by a IPTG, large quantities of the fusion protein are then able to be produced, not be detected in Western blots of bacterial lysates [14]. After induction with production of the antibody-pIII fusion protein in the absence of IPTG could antibody surface expression vector pSEX (fig. 1a, c), for example, the faster proliferating deletion mutants could quickly predominate. Using the particularly important during the amplification of antibody libraries since the production of the fusion protein when it is not required. This is in our choice of a phagemid system, however, was the possibility to repress and antibody protein can be produced for analysis. The major consideration opposed to phages for antibody expression is that large amounts of DNA or C-terminal domain of pIII [13-16]. One advantage of phagemids as the expression of single chain Fv or Fab fragments fused to the N-terminus Various phage and phagemid systems have now been constructed for so that only one of the three to five pIII sites is occupied by a fusion protein. The relative amounts of wild type pIII and fusion protein can be adjusted vector and a helper phage to provide packaging proteins and wild type pIII. fusions can be made with the C-terminal domain of pIII [12] using a phagemid fused near to the N-terminus of pIII do not affect its function. Alternatively, protein pIII of the M13 family of filamentous bacteriophages [11]. Peptides of presenting polypeptides on bacteriophages is provided by the docking

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/ the docking [11]. Peptides Alternatively, phagemid, wild type pIII, n be adjusted usion protein. instructed for the N-terminus phagemids as units of DNA consideration ility to repress ired. This is libraries since ite. Using the example, the of IPTG could nduction with be produced, identified by a ence between al sequences. high numbers uring antibody ible to isolate d cell sorter. eening assays prove to be get antibodies ument to the rein [17] (fig. hat functional e applicability 3 investigated.

AD, Winter G: played on phage.

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[illegible]

9. The library of claim 8 wherein said tag is a radioactive molecule, toxic molecule, or enzyme molecule.

10. The library of claim 7 wherein said antibodies or parts thereof are derived from humans, mice, rabbits, or chickens.

11. The library of claim 7 wherein said antibodies are chimeric antibodies with variable regions derived from one species and constant regions derived from another species.

12. The library of claim 11 wherein said chimeric antibodies have murine variable regions and human IgG1 constant regions.

13. The library of claim 7 wherein said antibodies are untagged antibodies.

14. The library of claim 13 wherein said untagged antibodies are Fv fragments.

15. The library of claim 13 wherein said untagged antibodies are single-chain Fv fragments.

16. The library of claim 13 wherein said untagged antibodies are Fab fragments.

17. The library of claim 13 wherein said untagged antibodies are F(ab)₂ fragments.

18. The library of claim 7 wherein said antibodies have been further modified by mutagenesis.

19. The library of claim 7 wherein said antibodies are chimeric antibodies with antibody variable regions attached to enzymes, T cell receptors, or portions thereof.

20. The library of claim 19 wherein said antibody variable regions are attached to enzymes.

21. The library of claim 7 wherein said antibody variable regions are attached to T cell receptors or constant regions of T cell receptors.

22. The library of claim 1, 2 or 3, wherein the library of receptor proteins has been modified from said parent library of receptor proteins by said members having a constant region from a different species than the variable regions.

23. The library of claim 1, 2 or 3, wherein the library of receptor proteins is a library of antibodies, and wherein said library has been modified from the parent library by comprising whole antibodies.

* * *

ferred in mass from a parent library of vectors to said library of vectors, wherein the vectors of said library of vectors have been modified, relative to the vectors of said parent library of vectors, by addition, subtraction, or substitution of coding sequences, and wherein said parent library of vectors has been selected in mass, for a subset of binding domains from a grandparent library of vectors, without characterization of all individual members of said grandparent library of vectors before said transfer from said parent library of vectors to said library of vectors without individual characterization of all members.

2. A library of recombinant receptor proteins wherein each receptor protein contains a pair of variable regions, wherein the variable regions of each pair associate with each other to form a binding domain, and wherein the totality of variable regions in said library of receptor proteins is diverse forming a library of variable regions, wherein said library of variable regions has been transferred in mass from a parent library of receptor proteins to said library of receptor proteins, wherein the receptor proteins of said library of receptor proteins have been modified, relative to the receptor proteins of said parent library of receptor proteins, by addition, subtraction, or substitution of sequences.

3. The library of claim 2 wherein said parent library of receptor proteins has been selected in mass, from a grandparent library of receptor proteins, for a subset of binding domains before said transfer from said parent library of receptor proteins to said library of receptor proteins.

4. The library of receptor proteins of claim 1, 2 or 3 wherein said receptor proteins are specific for one or more antigens.

5. The library of receptor proteins of claim 1, 2 or 3 wherein said receptor proteins are soluble proteins.

6. The library of receptor proteins of claim 1, 2 or 3 wherein said receptor proteins are cell surface proteins.

7. The library of receptor proteins of claim 1, 2 or 3 wherein said receptor proteins are antibodies of one or more isotypes selected from the group of isotypes consisting of IgG, IgM, IgA, IgE, and IgD.

8. The library of claim 7 wherein said antibodies are labeled with tags that facilitate detection and/or therapy.

conjunction-

(! ! !) MOLECULE TYPE: DNA (genomic)

(* !) SEQUENCE DESCRIPTION: SEQ ID NO:7:

SECRET

(2) INFORMATION FOR SEQ ID NO:8:

(!) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs

(B) TYPE: nucleic acid

(D) TOPOLOGY: UNCEN

(x i) SEQUENCE DESCRIPTION: SEQ ID NO:8:

0010 1400000000 0100000000

(2) INFORMATION FOR SEQ ID NO:9:

(!) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 42 base pairs

(B) TYPE: nucleic acid

(D) Topology: first

(* !) SEQUENCE DESCRIPTION: SEQ ID NO:9:

CCITCAACCAOC TAACOCITCAO ATTCAOACTC OAGAAOCTGA AC

24

(2) INFORMATION FOR SEQ ID NO:10:

(!) SEQUENCE CHARACTERISTICS:

(B) TYPE: **STRAND** **STRAND**

(b) Information: unknown

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(2) INFORMATION FOR SEQ ID NO:11:

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(B) LIFE: LIVING BEING

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I claim:

1. A method for preparing a first library of expression vectors comprising paired nucleic acid fragments, said paired nucleic acid fragments being suitable for transfer to prepare a second library of different expression vectors. 60

(a) observing a plurality of nucleic acid fragments wherein each nucleic acid fragment encodes a variable region or part thereof or a protein which contains said variable region;

(b) producing a plurality of nucleic acid segments, wherein each segment comprises a pair of different

(c) cloning said plurality of nucleic acid segments into first circular vectors to produce a library of vector molecules;

ment permitting expression of said nucleic acid fragments in a first host cell;

(c) introducing said first library of expression vector molecules into the first host cells under conditions and time sufficient to express a first library of polypeptides, wherein each of the polypeptides contains a sequence encoded by one of said pairs of linked nucleic acid fragments; and

(f) isolating said first library of expression vector molecules from said first host cells.

2. The method of claim 1, which further comprises isolating the plurality of segments comprising said first cassette from said first library of expression vectors molecules, and inserting said plurality of segments comprising said first cassette into a plurality of second vectors to produce a second library of expression vector molecules.

3. The method of claim 1, which further comprises exchanging said first cassette from an expression vector of said isolated first library of expression vector molecules with a second cassette, wherein said second cassette contains at least one promoter element permitting expression of said nucleic acid fragments in a second host cell.

4. The method of claim 2, which further comprises exchanging said first cassette from an expression vector of said second library of expression vector molecules with a second cassette, wherein said second cassette contains at least one promoter element permitting expression of said nucleic acid fragments in a second host cell.

5. The method of claim 2, wherein said second library of expression vector molecules is introduced into a plurality of second host cells.

6. The method of claim 4, wherein the second vector is a circular vector.

7. The method of claim 5, wherein said first host cell is a prokaryotic cell and said second host cell is a eukaryotic cell.

8. The method of claim 5, wherein said first host cell is a eukaryotic cell and said second host cell is a second eukaryotic cell.

9. The method of claim 5, wherein said first host cell is a prokaryotic cell and said second host cell is a second prokaryotic cell.

10. The method of claim 5, wherein said first host cell is a eukaryotic cell and said second host cell is a prokaryotic cell.

11. The method of claim 1, wherein said protein is a secreted protein or receptor protein.

12. The method of claim 11, wherein the secreted or receptor protein is selected from the group consisting of an antibody and a T-cell receptor.

13. The method of claim 1, wherein one nucleic acid fragment of each segment of said plurality of nucleic acid

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segments encodes a heavy chain variable region of an antibody and the other nucleic acid fragment of the segment encodes a light chain variable region of the same antibody.

14. The method of claim 1 wherein said nucleic acid fragments comprise a polyclonal population encoding variable regions or portions thereof of proteins selected from the group consisting of antibodies, T-cell receptors, B-cell receptors, natural killer cell receptors, macrophage receptors and combinations thereof derived from a polyclonal cell population.

15. The method of claim 14, wherein the proteins are selected from antibodies or T-cell receptors.

16. The method of claim 1 wherein the first cassette contains two promoters in opposite transcriptional orientations.

17. The method of claim 3 wherein the second cassette contains two promoters in opposite transcriptional orientations.

18. The method of claim 1, wherein said first cassette further comprises a nucleic acid sequence encoding a leader sequence of a secreted protein or membrane protein, and said nucleic acid sequence encoding said leader sequence is operably linked to a nucleic acid fragment of said pair of nucleic acid fragments.

19. The method of claim 3, wherein said first cassette further comprises a nucleic acid sequence encoding a leader sequence of a secreted protein or membrane protein, and said nucleic acid sequence encoding said leader sequence is operably linked to a nucleic acid fragment of said pair of nucleic acid fragments.

20. The method of claim 1, wherein said first circular vector is a prokaryotic or eukaryotic surface display vector or expression vector.

21. The method of claim 2 wherein said second vector is a circular vector.

22. The method of claim 21, wherein said second circular vector is a prokaryotic or eukaryotic surface display vector or expression vector.

23. The method of claim 1 wherein said polypeptides of step (c) are antibodies.

24. The method of claim 23, wherein said antibodies are chimeric antibodies.

25. The method of claim 24, wherein said chimeric antibodies have mouse variable regions and human constant regions.

26. The method of claim 1, wherein step (f) includes a preliminary screening step to select desired expression vector molecules and thereby reduce the number of expression vector molecules used in preparation of said second library from those used in said first library.

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